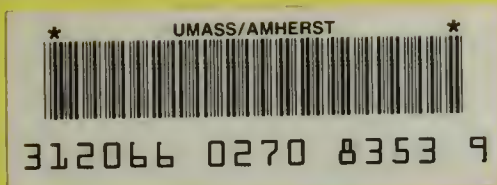


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DOCUMENTATION
FOR THE
RISK ASSESSMENT SHORTFORM
RESIDENTIAL SCENARIO

Policy #WSC/ORS-142-92

October 1992

Massachusetts Department of Environmental Protection
Office of Research and Standards
and the Bureau of Waste Site Cleanup

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Governor

Daniel S. Greenbaum
Commissioner

RISK ASSESSMENT SHORTFORM RESIDENTIAL SCENARIO

Policy #WSC/ORS-142-92

The Department of Environmental Protection Policy #WSC/ORS-142-92 is a *package* of material which consists of three items:

- (1) Computer spreadsheet software entitled *Risk Assessment ShortForm - Residential Scenario* (1 disk);
- (2) A document entitled *User's Guide to the Risk Assessment ShortForm - Residential Scenario* (\approx 30 pages); and
- (3) A document entitled *Documentation for the Risk Assessment ShortForm - Residential Scenario* (\approx 450 pages).

This package makes available a software program and guidance intended to streamline the human health risk characterization required under the Massachusetts Contingency Plan (310 CMR 40.00). While this risk assessment tool has been developed primarily for use at c.21E sites where the current or foreseeable use includes residential use, it may be generalized to other high exposure situations or employed as a screening mechanism at other, non-residential locations. The information provided in this guidance may be used in whole or in part by the risk assessor.

James C. Colman, Assistant Commissioner
Bureau of Waste Site Cleanup

10/6/92
Date

Carol Rowan West, Director
Office of Research and Standards

October 6, 1992

Date

FOREWORD

RISK ASSESSMENT SHORTFORM - RESIDENTIAL SCENARIO

The *Residential ShortForm* is an optional tool which has been developed by the Massachusetts Department of Environmental Protection's Office of Research and Standards in conjunction with the Bureau of Waste Site Cleanup to fill a perceived need for a streamlined method of evaluating potential human health risks at state superfund sites.

The *ShortForm* is a *LOTUS 1-2-3* (or *Quattro Pro*) spreadsheet incorporating standard assumptions for a residential exposure and formulae which are used to estimate human health risk (including estimated Excess Lifetime Cancer Risks, Subchronic Hazard Indices and Chronic Hazard Indices). Forty-nine chemicals are currently incorporated in the *ShortForm*. The *Residential ShortForm* evaluates potential exposures via direct contact with soil, ingestion of garden fruits and vegetables, use of drinking water and inhalation of indoor air. The only site specific parameters required to run the *ShortForm* are the exposure point concentrations for soil, drinking water and/or indoor air. The output of the *Residential ShortForm* is a package of eight summary tables which describe the exposure point concentrations, toxicity information and potential chemical-specific, medium-specific and total health risks. These tables would be submitted as part of a site characterization report.

The MA DEP Office of Research and Standards has also prepared a *User's Guide to the Risk Assessment ShortForm* and a *Documentation for the Risk Assessment ShortForm - Residential Scenario*. The *Documentation...* details each assumption and equation contained in the *ShortForm*, develops Relative Absorption Factors and provides standardized Toxicity Profiles for each of the 49 chemicals.

While the *Residential ShortForm* was developed specifically to meet the requirements of the Massachusetts Contingency Plan (MCP) for the evaluation of state superfund sites, it has found several additional applications, including: the calculation of site-specific target cleanup levels; the evaluation of public water supply wells; the development of allowable concentrations for land applied septage sludge; as a screening tool for determinations of *No Further Action Required* (NFA); and as a teaching tool for university risk assessment courses.

The *Risk Assessment ShortForm*, all its companion documentation and other policies/information of interest will be made available to the public and the regulated community through the State Bookstore (617-727-2834), and via a dial-in computer bulletin board system (Modem #: 617-292-5546) being established for this purpose. Please call the Office of Research and Standards at (617) 292-5570 for more information.

The Office of Research and Standards maintains a mailing list of companies and individuals interested in the use of risk assessment in environmental regulation in Massachusetts. The ORS uses this list to inform the regulated community about anticipated changes in regulations or policies, updates of lists of standards and guidelines, and the publication of new documents. If you would like to add your or your company's name to the mailing list, please send a note to:

Massachusetts Department of Environmental Protection
Office of Research and Standards
ATTN: Risk Assessment Mailing List
1 Winter Street, 3rd FL
Boston, MA 02108

The policies and procedures established in this document are intended solely as guidance. They are not intended and cannot be relied upon to create any right, substantive or procedural, enforceable by any party in any administrative or judicial proceeding with the Commonwealth.

TABLE OF CONTENTS

	FOREWORD	i
1.0	PURPOSE	1
2.0	APPLICABILITY	3
2.1	Land Use	3
2.2	Exposure Scenarios	4
2.3	Adequate Site Characterization	4
2.4	ShortForm Uses	5
3.0	RISK ANALYSIS PROCESS	9
3.1	Risk Assessment	10
3.2	Risk Management	11
4.0	MCP RISK ANALYSIS REQUIREMENTS	13
4.1	Risk Assessment	13
4.2	Risk Management	15
5.0	CURRENT AND REASONABLY FORESEEABLE USE	17
5.1	Land Use Is Residential	18
5.2	Groundwater Use	19
5.3	Universe of Applicable Sites	20
6.0	HAZARD IDENTIFICATION	21
6.1	Identification of Extent of Release of OHM	22
6.2	Elimination of OHM from the Risk Assessment	23
6.3	Comparison to Background Levels	24
6.4	Toxicity Profiles	37

TABLE OF CONTENTS, *continued...*

7.0	DOSE RESPONSE ASSESSMENT	39
7.1	Basic Assumptions	39
7.2	Sources of Dose-Response Information	42
7.3	Toxicity Information Summary Tables	44
8.0	EXPOSURE ASSESSMENT	51
8.1	Introduction	51
8.2	Basic Approach/Assumptions	51
8.3	Receptors	52
8.4	Potential Exposure Pathways	57
8.5	Pathways Evaluated	58
8.6	Exposure Point Concentrations	60
8.7	Soil - Direct Contact	66
8.8	Soil Particulates - Inhalation	79
8.9	Drinking Water - Inhalation, Dermal Contact and Ingestion	86
8.10	Homegrown Fruits and Vegetables	92
8.11	Vapors - Indoor Air	107
9.0	RISK CHARACTERIZATION	111
9.1	Purpose	111
9.2	Comparison of EPC To Standards	112
9.3	Hazard Index	113
9.4	Excess Lifetime Cancer Risk	117
9.5	Total Site Risks	121
9.6	Results - SUMMARY TABLES	123

TABLE OF CONTENTS, *continued...*

10.0	CONCLUSIONS	127
10.1	When No Further Remedial Response Action Is Necessary	128
10.2	When A Remedial Response Action Is Necessary	128
10.3	Phase II Health Risk Characterization Conclusion	129
10.4	Safety, Public Welfare And The Environment	130
11.0	UNCERTAINTY ANALYSIS	131
11.1	Narrative Discussion	131
11.2	Sources Of Uncertainty	132
11.3	Impacts Of Uncertainty On Risk Estimates	134
11.4	Just How Conservative Are We?	136
12.0	REFERENCES	137

APPENDICES

APPENDIX A -	GLOSSARY OF TERMS AND ACRONYMS
APPENDIX B -	TOXICITY SUMMARIES
APPENDIX C -	RELATIVE ABSORPTION FACTORS
APPENDIX D -	TOXICITY VALUES DERIVED BY THE MA DEP
APPENDIX E -	SOFTWARE LICENSE

LIST OF FIGURES

FIGURE NUMBER	TITLE	
6-1	Chromium in Soil - Massachusetts Background	28
6-2	Lead in Soil - Massachusetts Background	29
6-3	Nickel in Soil - Massachusetts Background	30
6-4	Zinc in Soil - Massachusetts Background	31
8-1	Soil Ingestion/Contact Rates vs Age	55
8-2	Water Intake vs Age	56
8-3	Homegrown Fruits and Vegetable Ingestion Rates vs Age	56
8-4	Mean Inhalation Rate vs Age	57

LIST OF TABLES

TABLE NUMBER	TITLE	
2-1	Applicability of the <i>Residential ShortForm</i> For Various Exposure Scenarios	4
5-1	Exposures For Residential Land Use	20
6-1	<i>Residential ShortForm</i> Chemicals	21
6-2	<i>Shortform</i> Soil Background Concentrations	27
6-3	Metals Concentrations in Eastern U.S. Soils	32
6-4	<i>Shortform</i> Indoor Air Background Concentrations	33
6-5	Indoor Air Concentrations (from Shah, 1988)	34
6-6	Indoor Air Concentrations (from Stolwijk, 1990)	35
6-7	<i>Shortform</i> Groundwater Background Concentrations	36
6-8	Metals Concentrations in Massachusetts Groundwaters	36
7-1	<i>ShortForm</i> Toxicity Values (Tables Printed from the <i>ShortForm</i>)	45
8-1	Summary of Soil Ingestion and Dermal Contact Rates	68
8-2	Indoor-Only Soil Ingestion Exposure	69
8-3	Calculation Of Age-Specific Soil Ingestion Rates	70

LIST OF TABLES, *continued...*

TABLE NUMBER	TITLE	
8-4	Calculation Of Time-Weighted Average Daily Soil Ingestion Exposures Normalized To Bodyweight	71
8-5	Calculation Of The Normalized Daily Soil Intake Rates Used In The <i>ShortForm</i>	72
8-6	Indoors Only - Dermal Contact	74
8-7	Indoors & Outdoors - Dermal Contact	75
8-8	Calculation Of Age-Specific Soil Dermal Contact Rates	76
8-9	Calculation Of Time-Weighted Average Daily Soil Dermal Contact Exposures Normalized To Bodyweight	77
8-10	Calculation Of The Normalized Daily Soil Dermal Contact Rates Used In The <i>Residential ShortForm</i>	78
8-11	Comparison Of Inhalation Of Particulates To Soil Ingestion Pathway	81
8-12	Comparison Of Inhalation Of Particulates To Soil Dermal Contact Pathway	82
8-13	Inhalation Pathway Exposure As A Percentage of Total Soil Exposure	83

LIST OF TABLES, *continued...*

TABLE NUMBER	TITLE	
8-14	Inhalation Of Particulates - Exposure Assumptions	85
8-15	Drinking Water - Exposure Assumptions	89
8-16	Chemicals And Their Assigned Drinking Water Usage Multipliers	91
8-17	Food Chain Analysis Contaminants Of Concern	93
8-18	Proportion Of Fresh Produce That Is Homegrown	94
8-19	Average Daily Intake Of Produce	95
8-20	Average Daily Intake Of <u>Homegrown</u> Produce	96
8-21	Average Daily Intake Of <u>Homegrown</u> Produce (II)	98
8-22	Plant Uptake Factors	101
8-23	Food Chain Multipliers	105
8-24	Ingestion of Food - Exposure Assumptions	106
8-25	Chemicals Included In The Indoor Air Exposure Pathway	107
8-26	Inhalation Of Indoor Air - Exposure Assumptions	109

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1.0 PURPOSE

This *Risk Assessment ShortForm - Residential Scenario* (also known as the *Residential ShortForm*) and accompanying documentation is presented by the Department of Environmental Protection as a tool for streamlining the assessment and remediation of disposal sites in the Ch. 21E waste site clean-up program. The *Residential ShortForm* will be part of a set of *ShortForms* which is expected to include a number of exposure scenarios, including Office/Commercial and Industrial/Construction spreadsheets. The *ShortForms* streamline the process by providing a rapid, low cost procedure for assessing health risks. The *ShortForms* are "off the shelf" packages containing procedures and assumptions which have already been approved by DEP for use in decision-making at many disposal sites.

Chapter 21E of the Massachusetts General Laws is the Massachusetts Oil and Hazardous Material Release Prevention and Response Act, which became law in 1983 and was amended as a result of citizens' initiative Number 4 in 1986, and by an act of the legislature in July, 1992. This risk-based statute identifies requirements for action at disposal sites and describes the liability issues related to disposal sites. The statute requires that the Department of Environmental Protection (DEP) ensure that actions be taken at disposal sites as necessary to eliminate or abate "significant or otherwise unacceptable risk of harm to health, safety, public welfare or the environment" associated with oil or hazardous materials (OHM).

The DEP promulgated the Massachusetts Contingency Plan in 1988. Those regulations provide the legally enforceable procedures for the implementation of the Ch. 21E statute. Subpart E of these regulations specifies, for disposal sites, a phased approach for assessing the nature and magnitude of releases of OHM and their associated risks as well as for the development and selection of remedial alternatives. If, in the absence of remediation, significant risk exists or would exist, considering reasonably foreseeable uses of the disposal site and surrounding environment that may be affected by OHM at the site or in the surrounding environment, then development, evaluation and selection of remedial alternatives is indicated. The statute requires that a "permanent solution" ultimately be implemented at all disposal sites requiring remediation. Such a solution eliminates significant risk for the foreseeable future.

In the Subpart E process, risk assessments can be conducted for three main reasons: first, to determine if remediation is needed; second, to identify target clean-up levels which meet the risk requirements; and third, to evaluate the effectiveness of remedial alternatives in eliminating significant health risk. Therefore, the *ShortForm* has been designed specifically for those purposes as described in the Phase II and Phase III sections of Subpart E.

The *ShortForm* should also be useful, provided there is adequate site information available, to evaluate if a No Further Action (NFA) determination is appropriate at other chronological points in the process. In particular, the *ShortForm* can be used to determine if Short Term Measures (STM) or Interim Measures (IM) have eliminated significant health risk. It should be noted that an NFA determination cannot be made solely on the basis of a health risk assessment - risks of harm to safety, public welfare, and the environment must also be evaluated. The *ShortForm* may also be used to develop criteria for making imminent hazard determinations based on health risk.

This version of the *Residential ShortForm* was developed for use under the existing Massachusetts Contingency Plan.

As a result of the July 1992 legislative amendments to M.G.L. Chapter 21E, the Department's Waste Site Cleanup program is currently being redesigned in a manner which will result in significant changes in the MCP. As these changes are implemented, the *Residential ShortForm* and its *Documentation* shall be revised to reflect the new program.

2.0 APPLICABILITY

This version of the *ShortForm* is intended for use at "residential" sites which are to be evaluated via the health risk assessment method set forth in section 40.545(3)(g)3.b. of the MCP, and described as a "*Method 3b*" risk characterization in the Department's *Guidance for Disposal Site Risk Characterization...* (MA DEQE, 1989a). Method 3b risk assessments are specifically for multi-media disposal sites. These multi-media situations are ones in which a given receptor is exposed to contaminant situations which would not normally be dealt with by a single medium-specific program within DEP. Examples of DEP medium-specific programs are the Division of Water Supply, the Division of Air Quality Control, and the Division of Water Pollution Control.

It is expected that a set of *ShortForms* will be developed to identify health- or risk-based guidelines for use in evaluating the risk of harm to human health for "single-medium" disposal sites evaluated via Method 3a of the MCP (40.545(3)(g)3.a). These guidelines may serve as health-based clean-up levels.

2.1 Land Use

The term "residential" does not limit the applicability of this *ShortForm* to those disposal sites currently in use as a residential property.

"Residential" disposal sites are those sites for which the current or reasonably foreseeable use has been determined to be residential (see Section 5.0), *or* those sites which are evaluated with an assumption that use could be residential (even though this use is not necessarily foreseeable); *or* sites "surrounded" by residential properties.

Examples of locations which could be evaluated with the *Residential ShortForm* include: single family homes, multiple family homes, condominiums, apartment complexes, and vacant lots adjacent to residential property.

Residential property does not necessarily involve SOIL exposure! If there is no accessible soil (either currently or for the foreseeable future), then soil exposures may not be counted as an exposure medium when determining if there is a multi-media site for which the short form is applicable.

2.2 Exposure Scenarios

The *Residential ShortForm* scenario applies to disposal sites where the receptor of concern may be exposed via one of the combinations of pathways described in Table 2-1. This figure describes the most common "multi-media" residential scenarios. It should be noted that the term "multi-media" should not be interpreted literally to mean where there is OHM in more than one medium. The term is used to refer to situations where the nature of combined exposures indicates that a single medium-specific program within DEP would not usually handle by itself. Therefore, a "multi-media" site is actually any site which is not a "single-medium" site - those sites which would normally be handled by one medium-specific program within DEP. Examples of those "single-medium" sites include: exposure to OHM from in-home use of drinking water only; exposure to OHM from indoor air vapors only.

Table 2-1

APPLICABILITY OF THE <i>RESIDENTIAL SHORTFORM</i> FOR VARIOUS EXPOSURE SCENARIOS	
MULTI-MEDIA SCENARIOS Use the <i>ShortForm</i>	SINGLE-MEDIUM SCENARIOS Do NOT Use the <i>ShortForm</i>
Soil and indoor air	Soil and vegetables
Soil and drinking water	Soil only
Soil, vegetables and indoor air	Indoor air only
Soil, vegetables and drinking water	Drinking water only
Soil, vegetables, indoor air and drinking water	Vegetables only
Drinking water and indoor air	
Drinking water and vegetables	

2.3 Adequate Site Characterization

As is the case with any health risk assessment activity, the risk assessment results can only be as meaningful as the site information which serves as the basis of the assessment. Therefore, in most circumstances, the *ShortForm* is applicable (in a formal regulatory sense) when the site has been adequately characterized. There are minimum information requirements which must be met before a *ShortForm* risk assessment can be conducted with the intent of using the results to characterize the health risks of the site for purposes of showing that "no significant health risk" exists.

USER HINT: One could use the *ShortForm* to conclude that remediation is required at a site without completely characterizing the site if there is enough information available to generate exposure point concentrations for some OHM which are present at significant concentrations OR by running lowest reported concentration for each OHM with risk estimates which exceed total site risk limits. The latter approach could be used to determine that remediation is required, but it would not necessarily be an adequate baseline health risk assessment.

The minimum information requirements for conducting a *ShortForm* risk assessment, the results of which would be used as an official health risk characterization for Phase II, Phase III, or for an NFA demonstration after an STM or an IM include (but are not limited to):

1. Nature and extent of the release(s) of OHM fully characterized.
2. All migration pathways for OHM released fully characterized.
3. All current and potential receptors or receptor groups identified.
4. All activities likely to occur at the location identified. For current and foreseeable uses of land and waters.
5. Exposure points have been identified.
6. Representative sampling and analysis of environmental media at exposure points has been conducted.
7. Background levels of OHM in appropriate media have been identified.

Section 40.545 of the MCP should be consulted to expand upon the information needs listed above.

2.4 ShortForm Uses

2.4.1 Rough Screening

A rough screening may be conducted to get a general picture of the seriousness of a site. This would be done when some site information is available, but the site is not "adequately" characterized. One could determine that a site definitely requires remediation, may require remediation, or is unlikely to require remediation. Such an analysis could use lowest reported concentrations of each OHM in each exposure pathway, average or mid-range values, or highest reported concentrations of each OHM in each exposure pathway respectively. Such a screening evaluation could not be used to make a No Further Action determination since the site characterization is incomplete or otherwise inadequate.

2.4.2 Phase II Baseline Health Risk Characterization

The *ShortForm* has been developed specifically for the purpose of conducting a baseline health risk characterization as required in section 40.545(3)(g)3.b. For "multi-media" sites which have been adequately characterized per the other requirements of 40.545, the *ShortForm* is used to conduct the appropriate risk characterization which serves, in part, as the basis for decisions concerning the need for remediation. Representative exposure point concentrations are inputs to the *ShortForm*.

2.4.3 Phase III Derivation of Target Clean-up Levels

The *ShortForm* can be used, for multi-media sites, to identify combinations of chemical and medium-specific concentrations which would meet applicable standards and Total Site Risk Limits. At a given site, there may be an infinite number of combinations which could meet the Total Site Risk Limits. In those cases, target concentrations can be developed in a way which maximizes risk reduction and minimizes cost. It can also identify situations where background concentrations prevent achievement of the Total Site Risk Limits.

2.4.4 Phase III Evaluation of Effectiveness of Remedial Alternatives

When remedial alternatives utilizing known technologies are proposed, it is often possible to project the effectiveness of those technologies in reducing exposure point concentrations. When the capability of a given technology is described in terms of likely residual exposure point concentrations, then those concentrations can quickly be evaluated by the *ShortForm* to determine if that technology alone is capable of achieving the Total Site Risk Limits.

2.4.5 No Further Action after STM or IM

Short Term Measures (STM) and Interim Measures (IM) often reduce concentrations of OHM at exposure points, prevent additional migration of OHM to exposure points, or prevent access to exposure points. Subsequent to the completion of such measures, it may be appropriate to evaluate the risks which remain. The *ShortForm* can perform this evaluation provided adequate exposure point concentrations which are representative of foreseeable exposures can be identified based on post-STM or post-IM sampling and analytical results. The *ShortForm* addresses only health risk, but a No Further Action demonstration must also show that there is no significant or otherwise unacceptable risk of harm to safety, public welfare and the environment.

2.4.6 Derivation of Method 3A clean-up levels

At "single-medium sites", Method 3.a. is used to assess human health risks. That method utilizes, where they exist, applicable or suitably analogous public health standards, guidelines and policies to evaluate the significance of exposure point concentrations. Where such a standard, guideline, or policy does not exist for an OHM of concern, a health- or risk-based guideline is to be developed. Each chemical- and medium-specific guideline "shall be set so that the daily receptor dose resulting from exposure to the concentration specified in the guideline shall not exceed twenty percent (20%) of the appropriate Reference Dose or other allowable daily dose specified by the Department and shall not be associated with an excess lifetime cancer risk greater than one in one million."

The *ShortForm* can be used in an iterative manner to identify such health- or risk-based guidelines for individual OHM. This is most easily accomplished one chemical at a time. By entering one value in the data input section for either soil, drinking water or indoor air for a given chemical and viewing the Risk Summary table (not the medium-specific summary table), it is possible in a couple of minutes to identify the concentration which meets the guideline requirements specified in the MCP. Subsequent versions of the *ShortForm* may include an option to automatically calculate such guidelines.

2.4.7 Evaluation of the existence of Imminent Hazards to Health

The Department is currently developing specific criteria which will be used to determine what situations constitute an imminent hazard to health. In the near future, it may be possible to use the *ShortForm* as part of the Imminent Hazard evaluation process.

For example, if the total excess lifetime cancer risk for an assumed lifetime exposure associated with contamination in an operating water supply (public or private) exceeds one in ten-thousand, that water could be deemed unsuitable for any residential use per the procedures in "Guide to the Regulation of Toxic Chemicals in Massachusetts Waters" (MA DEP, 1990a).

The Drinking Water Summary Table from the *ShortForm* would contain the ELCR estimate which would be compared to such a risk management criterion.

2.4.8 Use of *ShortForm* as Part of a Larger Assessment

The *ShortForm* results by themselves adequately characterize health risks for a receptor or receptor group only if that receptor has no exposure pathways which are not included in the *ShortForm*. In circumstances where a receptor or receptor group has additional exposure pathways not included in the *ShortForm*, the *ShortForm* could still be applicable, provided the additional exposure pathways are evaluated and the risks for those pathways are combined with the risk estimates from the *ShortForm* to calculate Total Site Risks.

3.0 RISK ANALYSIS PROCESS

Environmental protection often involves the regulation of situations which pose risks to human health, safety, public welfare or the environment. During the last decade, achieving the goals of environmental protection have increasingly relied on the process of *risk analysis*. Risk analysis encompasses a broad array of techniques, combining the disciplines of science, engineering and statistics to estimate and evaluate the probability and magnitude of health or environmental risk. Given the frequent limitations in available, relevant information, the challenge in risk analysis has been to make the best possible use of data and expert assumptions or judgments to estimate adverse affects and determine appropriate measures of protection.

The term Risk Analysis has often been used synonymously with risk assessment. However, it is important to recognize that risk analysis involves both methods of risk assessment as well as methods to use the resulting information for environmental decision making. This latter process is often referred to as *risk management*.

The National Research Council (NRC, 1983) in the widely accepted and often quoted document, **Risk Assessment in the Federal Government: Managing the Process** describes the process of risk analysis and provides insight into the relationship and distinction between risk assessment and risk management. In that document, the NRC describes the two distinct elements of risk analysis as follows:

Regulatory actions are based on two distinct elements, risk assessment, the subject of this study, and risk management. Risk assessment is the use of the factual base to define the health effects of exposure to individuals or populations to hazardous materials and situations. Risk management is the process of weighing policy alternatives and selecting the most appropriate action, integrating the results of risk assessment with engineering data and with social, economic and political concerns to reach a decision.

More recently, the Council on Environmental Quality (CEQ, 1989) explored the use of risk analysis as a regulatory framework in the publication **Risk Analysis: A Guide to Principles and Methods for Analyzing Health and Environmental Risks**. The following discussions of risk assessment and risk management are drawn from these documents to clarify the use of risk analysis techniques in environmental protection and the investigation and cleanup of hazardous waste sites in Massachusetts (see Section 4.0 - Risk Analysis Requirements).

3.1 Risk Assessment

The risk assessment process defined by the NRC generally describes the methods employed by the Commonwealth of Massachusetts and the federal government for the regulation of environmental contaminants. According to the NRC, the risk assessment process involves four steps: hazard identification, dose-response assessment, exposure assessment and risk characterization.

Hazard Identification determines whether a substance causes adverse effects and identifies those effects. This step describes why the substance is of regulatory concern.

The *Dose-Response Assessment* describes the relationship between the level of exposure and the likelihood and/or severity of an adverse effect. Simply speaking, the dose-response information describes the toxicity of the substance.

The *Exposure Assessment* involves identifying potential routes of exposure; characterizing the populations exposed; and determining the frequency, duration and extent of exposure.

The last step of the risk assessment process is the *Risk Characterization* which combines information from the other three steps to describe the type (e.g., carcinogenic or non-carcinogenic) and magnitude of risks to exposed populations. It also identifies the uncertainty in the characterization of risks. The results of any risk assessment reflect scientific uncertainty resulting from limitations in available data and assumptions that are made in the absence of such data. These assumptions and limitations should be discussed.

Each of these risk assessment steps as it applies to the *Residential ShortForm* is described in detail in separate sections of this document.

It is important to remember that risk estimates generated in the risk assessment are not measures of actual or absolute risks. Rather, risk assessments are a tool - a method of providing valuable information regarding potential risks to public health and the environment. Risk assessment is used throughout the regulatory process to provide such information, whether it is to determine "How clean is clean enough?" at a waste disposal site, to develop drinking water standards for public water supplies, or to evaluate a proposed facility seeking a source permit.

While *ideally* risk assessment is an objective analytic process based solely on scientific considerations, subjective decisions are often made when available evidence is not conclusive

or when assumptions need to be made. These judgments inevitably draw on both scientific and policy decisions. The NRC makes a point to distinguish between these risk assessment policy judgments from "judgments and choices from the broader social and economic policy issues that are inherent in risk management decisions." It has long been recognized that some of the controversy surrounding regulatory decisions such as what level of cleanup at a site is appropriate, have resulted from a blurring of the distinction between the process of risk assessment and risk management.

3.2 Risk Management

If risk assessment gives us the answer to the question "*What is the risk?*" then **risk management** is the method for determining what to do about it. Risk management is the decision-making process that usually considers the risk assessment results along with any relevant political and social values and economic or engineering information. According to the NRC, risk management involves three steps: development and evaluation of regulatory options, selection and implementation of one or more options, and evaluation of the effectiveness of the selected option or options.

This decision-making process necessarily requires the use of value judgments on such issues as the acceptability of the risks and the reasonableness of the costs of control. Social and political considerations may vary from community-to-community and from year-to-year. Factors such as engineering feasibility, while considered to be somewhat more objective, still may change as technology progresses. In any event, it is not surprising and should be expected that regulatory programs operating under different legislative mandates and addressing various environmental contamination situations appear to require inconsistent levels of control when measured by residual risk alone. Remember that the health risk assessment is only one piece of information considered in the risk management process.

People perceive risks differently depending on the nature of the risks, their individual experiences and the social, political or cultural context of the risk. Risk perceptions are influenced by whether they have voluntarily agreed to bear them and whether or not they have control over the source and management of the risks, and trust in those seen as responsible for the risk or control of risks. Other factors affecting risk perception and ultimately "acceptability" include such issues as fairness, equity, and the distribution of risks versus benefits. These differences in risk perception may not affect the risk assessment process, but clearly they can have impacts on the management and communication of risks.

Thus concepts such as "significant risk" or "acceptable risk" do not have universal definitions, nor are the definitions necessarily based solely on risk assessment. Many factors go into the definition of "significant risk" which should be considered part of the risk management decision.

The next section examines the specific legislative mandates of M.G.L. Chapter 21E and the regulatory requirements of the Massachusetts Contingency Plan.

4.0 MCP RISK ANALYSIS REQUIREMENTS

The Massachusetts Oil and Hazardous Material Release Prevention and Response Act, Massachusetts General Laws Chapter 21E (the statute) sets forth requirements for the assessment and remediation of State Superfund sites. The statute requires that "permanent solutions" be achieved at all disposal sites, a permanent solution being defined as one that achieves, at a minimum, a level of "no significant risk". Permanent solutions must eliminate any significant or otherwise unacceptable risk of harm to health, safety, public welfare or the environment during any foreseeable period of time, and reduce concentrations of oil or hazardous materials to levels which would exist in the absence of the disposal site when feasible.

The Massachusetts Contingency Plan (MCP) was promulgated under Chapter 21E on October 3, 1988. Similar to the National Contingency Plan (NCP) under the federal Superfund program, the MCP sets forth the specific requirements to implement Chapter 21E. The MCP establishes requirements and procedures for identifying, evaluating and cleaning up releases of oil or hazardous materials to the environment.

4.1 Risk Assessment

The MCP specifies a risk assessment process that is consistent with the methods adopted by the EPA for use on federal Superfund sites. While the basic approach and methodology for performing risk assessments is similar in both the state and federal program, the definition of what constitutes a "significant" risk or answers the question "how clean is clean" is unique to Massachusetts. This difference is, in fact, the result of specific risk management decisions, and is discussed further in Section 4.2 below.

Under the MCP, the assessment and remediation of Chapter 21E disposal sites is carried out in a phased approach. As stated at 310 CMR 40.545, the Phase II - Comprehensive Site Assessment has three objectives:

- characterize the type and quantity of oil or hazardous materials released at or from the disposal site;
- characterize and evaluate the risk of harm that the disposal site poses to human health, safety, public welfare, and the environment; and
- provide data necessary to develop remedial response alternatives as required in 310 CMR 40.546 (Phase III).

Phase II investigations collect information to support development of a risk characterization. The purpose of the characterization is to evaluate the extent to which compounds present at a site present or may present a significant risk to health, safety, public welfare or the environment within the meaning of the MCP. The Phase II risk characterization process provides a framework for determining (1) whether remediation at a disposal site is required; and (2) the extent of remediation needed to maintain a temporary or permanent solution.

To provide more detailed guidance on how Phase II risk characterizations are performed, DEP published a guidance document - **"Guidance for Disposal Site Risk Characterization and Related Phase II Activities - in support of the Massachusetts Contingency Plan"** (MA DEQE, 1989a). The guidance document focuses primarily on the characterization of the risk to human health. The evaluation of risk to safety, public welfare and the environment currently relies upon the comparison of site specific conditions to existing standards and guidelines.

To recognize the variability of conditions commonly found at disposal sites, the MCP and the Guidance Document describe four methods that can be used to characterize risk of harm to human health at disposal sites. Only one of the four methods for characterizing risk is appropriate for a given disposal site, and the *Guidance Document* should be consulted for criteria to be used in method selection. The *Residential ShortForm* has been designed to meet the requirements of a Method 3b (multi-media) human health risk characterization required under the MCP, although it may have additional applications (Section 2.4).

Method 3b is appropriate when human receptors may be exposed to the oil or hazardous materials (OHM) at or from the disposal site by more than one contaminated media, and if there are not existing standards applicable to each OHM in every medium to which persons might be exposed, or specific promulgated sets of cleanup levels for the site category.

In Method 3b, exposure point concentrations are compared to applicable or suitably analogous public health standards promulgated under existing regulations, and in addition, a site specific risk assessment is conducted. The results of the risk characterization are threefold: (1) documentation of any comparisons to standards which were conducted, (2) an estimate of Total Excess Lifetime Cancer Risk for each receptor group associated with the disposal site, and (3) estimate(s) of Total Site Non-cancer Risk (as measured by a Hazard Index) for each receptor group associated with the disposal site.

The *ShortForm Risk Assessment - Residential Scenario* can be incorporated into the site-specific risk characterization required at the end of the MCP Phase II Investigation. The *Residential ShortForm* is a lower cost option and a rapid tool that can be used to estimate risks (both cancer and non-cancer) for a residential receptor assumed to live on or near a disposal site. The *ShortForm* results are calculated in a manner consistent with guidance

published by the Department (MA DEQE, 1989a) and may be directly compared to the MCP risk management criteria (risk limits) detailed in 310 CMR 40.545(3)(g)3.b. and described in Section 4.2 below.

4.2 Risk Management

While risk assessment and risk management are two distinct processes, how and when they are applied can vary depending upon the application or circumstances. Oftentimes the two steps overlap, but it is still important to recognize the differences. The risk assessment gives us information on the level of risk associated with exposures at a site. The risk management process defines whether those risks are considered "significant", and thus require remediation. If remediation is necessary, the risk management process defines the level of remediation required to achieve a *permanent* or *temporary solution*.

Permanent solution is defined in the statute and regulations, and the attainment of a *permanent solution* requires the elimination of "significant risk" of harm to human health, safety, public welfare and the environment for all current and foreseeable future uses of the disposal site and surrounding area. In addition, a *permanent solution* should reduce, to the extent possible, the level of oil or hazardous material in the environment to the level that would exist in the absence of the disposal site - commonly referred to as "background". A *temporary solution* must be implemented if a permanent remedy is not feasible at the present time. A *temporary solution* eliminates "significant risk" until a *permanent solution* is in place. While "Significant Risk" has no universal definition, the enactment of Chapter 21E and the promulgation of the Massachusetts Contingency Plan required that the Department provide a working definition. This definition forms the basis of the risk management decisions at disposal sites.

Consistent with M.G.L. Chapter 21E, a risk management philosophy was developed for the MCP which: (1) recognized the legislative and referendum mandate to protect human health, safety, public welfare, and the environment, (2) was consistent with existing state regulatory programs, and (3) restored sites to background conditions whenever feasible. The MCP risk characterization process was designed to ensure that this risk management philosophy is consistently applied at all disposal sites.

Central to the Method 3b risk characterization process is the comparison of estimated Total Site Risks to the Total Site Risk Limits contained in the regulations. These risk limits, in combination with any applicable or suitably analogous standards, essentially define whether a site poses a significant risk to human health. The Total Site Cancer Risk Limit is one in one hundred thousand (1×10^{-5}); the Total Site Non-cancer Risk Limit is a Hazard Index equal to 0.2.

The MCP is explicit in its interpretation of the significance of the risk estimates. The risk management philosophy inherent in the establishment of the risk limits is to ensure that no potential receptor groups would experience an excess lifetime cancer risk greater than the risk limit, regardless of the number of chemicals or exposure routes that exist at a site. The noncancer risk limit reflects a risk management decision that exposures related to a disposal site not contribute more than 20% of an estimated "allowable" dose - a dose which would not result in adverse health effects. This 20% *source allocation* reflects the fact that everyone is exposed to chemicals at home, at work and play, and in the ambient air. It ensures that the combination of site- and non-site-related exposures would not be likely to result in adverse health effects.

The risk based approach is clearly the foundation for disposal site cleanup decisions. Remediation of the disposal site is required if: (1) Exposure Point Concentrations exceed any applicable or suitably analogous public health standards, *or* (2) the estimated cancer or non-cancer risks associated with exposure to OHM at or from the disposal site exceed the Total Site Risk Limits (310 CMR 40.545(3)(i)). Remedial alternatives must be evaluated to determine if they eliminate "significant risk" as defined in the MCP (310 CMR 40.546).

The *Residential ShortForm* was developed to provide the site manager, site owner, DEP staff or the general public with a risk assessment tool which is compatible with the risk management criteria contained in the Massachusetts Contingency Plan. The *ShortForm* can be used to determine the need for remediation by comparing Exposure Point Concentrations to standards and the estimated Total Site Risks to the MCP Total Site Risk Limits. Remedial Alternatives may also be identified and target cleanup levels developed in a manner which clearly demonstrates that they meet the MCP risk management criteria.

The risk management criteria described in this section concerns the potential risk of harm to human health. Under the Massachusetts Contingency Plan remediation is also required to eliminate any "significant risk" to safety, public welfare or the environment. Such risks must be identified and evaluated per the MCP, and are part of the selection criteria for remedial alternatives.

The *Residential ShortForm* estimates only the risk of harm to human health, and can not be substituted for the entire risk characterization required under the MCP. Specifically, the *ShortForm* meets the requirements of 310 CMR 40.545(3)(g), and does not fulfill the requirements of 310 CMR 40.545(3)(h).

5.0 CURRENT AND REASONABLY FORESEEABLE USE

The ultimate goal of the site assessment and remediation process mandated under M.G.L. Chapter 21E and the Massachusetts Contingency Plan is the attainment of a "*permanent solution*" which is protective of public health, safety, welfare and the environment. By definition such a permanent solution must consider not only the current use of the site and the surrounding area, but also any uses which may occur in the reasonably foreseeable future.

LAND USE

The *Risk Assessment ShortForm - Residential Scenario* has been developed for disposal sites whose current and/or reasonably foreseeable future land use is determined to be residential.

GROUNDWATER USE

The *Residential ShortForm* may be used to evaluate disposal sites for which the current and/or foreseeable future use of the groundwater *either* is or is not drinking water.

The current and reasonably foreseeable uses of a site and the surrounding area help define the potential receptor groups which must be evaluated and the activities by which they may be exposed to the oil or hazardous materials. (It may be helpful to think of the term "*use*" as relating to activities and exposure which may occur at a given location, rather than as a zoning or urban planning term.) The determination of use plays a role in both the *baseline* risk assessment and the selection of the remedial alternative. The baseline risk assessment (performed as part of the Phase II investigation) answers the question "*What are the potential human health risks associated with this site as it stands now and if it were to remain unremediated into the future?*" Remedial alternatives must be evaluated (in Phase III) to determine if they eliminate significant risk for the current and future uses of the site and the surrounding area.

As part of the Waste Site Cleanup program redesign, the Department is developing a policy which will assist a site manager in determining the reasonably foreseeable future use of a site and surrounding area.

Determinations of current and future use must be made for both the use of the land and the groundwater, and these determinations are independent of each other. Table 5-1 lays out some possible exposure combinations of residential land use and groundwater use.

While the *Residential ShortForm* is intended for the evaluation of the residential use of a disposal site, there is some flexibility within this use category to tailor the evaluation considering site-specific exposures. The following sections briefly describe the options available to the risk assessor within the limits of the residential use of the location.

5.1 Land Use Is Residential

5.1.1 Potential For Soil Contact

For disposal sites where there is potential for direct soil contact, the *Residential ShortForm* version 1.6a assumes that exposure to the potential residential receptor will occur via the incidental ingestion of soil, dermal contact with the soil, and via the ingestion of fruits and vegetables grown in the soil. (Version 1.6b assumes the same potential exposures with the *exception* of the ingestion of homegrown fruits and vegetables.) Exposure assumptions (described in Section 8.7) consistent with the residential use of the location were developed for this scenario and are embedded in the spreadsheet. These assumptions cannot be modified by the risk assessor.

If the ingestion of homegrown fruits and vegetables can be eliminated as a pathway (either by documenting site-specific conditions which would prevent gardening or the imposition of institutional controls which could effectively restrict such gardening), then the *Residential ShortForm* version 1.6b would be considered for use. Version 1.6b can be used to assess risks associated with direct contact with contaminated soil, use of contaminated drinking water and/or inhalation of contaminated indoor air.

For those disposal sites with no potential of exposure to contaminated soils, the direct contact pathways (soil ingestion and dermal absorption) and the homegrown fruits and vegetables pathway may be eliminated from consideration. In this case no soil exposure point concentrations would be entered into the spreadsheet. There may be "no potential of exposure to contaminated soils" for a number of reasons, including: (1) the soil is considered to be uncontaminated or (2) the contaminated soil is completely covered by a building.

5.1.2 Indoor Air

Indoor air exposures are evaluated based upon residential exposure assumptions (described in Section 8.11) for those disposal sites which have been impacted by volatile organic compound (VOC) contamination. These exposure assumptions are embedded in the spreadsheet and cannot be modified by the risk assessor.

For those disposal sites which have no potential current or future indoor air impacts, this exposure pathway may be eliminated from consideration. In this case no indoor air concentrations would be entered into the spreadsheet.

5.2 Groundwater Use

As part of the Waste Site Cleanup program redesign, the Department is developing guidance on determining the current and foreseeable use of groundwater, and on the applicability of the Department's groundwater standards. The *Documentation for the Residential ShortForm* will be revised as this guidance is completed.

5.2.1 Groundwater As Drinking Water

If the current or foreseeable use of the groundwater is determined to be drinking water, then the potential exposures associated with the use of that water are evaluated. The exposure assumptions incorporated in the drinking water pathway (described in Section 8.9) are consistent with the residential use of the site. These assumptions are embedded in the spreadsheet and cannot be modified by the risk assessor.

5.2.2 Groundwater Is NOT Used As Drinking Water

If the current and foreseeable future use of the groundwater is determined not to be drinking water, then this exposure pathway may be eliminated from the assessment. In this case no groundwater concentrations of OHM would be entered into the spreadsheet.

5.3 Universe Of Applicable Sites

As described above and in Section 2.0, the *Residential ShortForm* may be considered applicable at a wide range of disposal sites which would fall under the general category of "residential use". The following table (Table 5-1) describes nine (9) general residential site types based upon their potential for exposure. Only the "multi-media" types would be evaluated via the *Residential ShortForm*. Table 2-1 delineates the applicability of the *Residential ShortForm* for various exposure scenarios.

Table 5-1

EXPOSURES FOR RESIDENTIAL LAND USE		
GROUNDWATER USE		
RESIDENTIAL LAND USE	DRINKING WATER	NOT DRINKING WATER
	drinking water soil, direct contact soil, gardening indoor air	soil, direct contact soil, gardening indoor air
	drinking water soil, direct contact soil, gardening	soil, direct contact soil, gardening *
	drinking water soil, direct contact	soil, direct contact *
	drinking water indoor air	indoor air *
	drinking water *	-
* These sites would not be evaluated using the "multi-media" ShortForm, as they are "single-medium" (Method 3a) situations.		

6.0 HAZARD IDENTIFICATION

For any disposal site being evaluated with the *Residential ShortForm*, hazards associated with OHM located at the disposal site and the surrounding environment must be described as part of the risk assessment process. The Hazard Identification section identifies the OHM present at the disposal site, summarizes the analytical data which has been collected, and describes the potential health effects which may be associated with exposure to these materials. The *Residential ShortForm* currently lists 49 chemicals for which a quantitative risk assessment may be performed. These chemicals were selected on the basis of their frequency of occurrence at c.21E sites, and it is expected that additional chemicals will be added to the *ShortForm* as it is updated. Users of this tool are encouraged to submit suggestions for chemicals to add. The current *Residential ShortForm* chemicals are listed in Table 6-1.

Table 6-1

<i>Residential ShortForm</i> Chemicals		
Metals & Inorganics (10)	VOCs & SVOCs (22)	PAHs (17)
Arsenic	Benzene	Acenaphthene
Cadmium	Bis(2-ethylhexyl)	Acenaphthylene
Chromium	Phthalate	Anthracene
Lead	Carbon Tetrachloride	Benzo[a]anthracene
Mercury	Chlorobenzene	Benzo[a]pyrene
Nickel	Chloroform	Benzo[b]fluoranthene
Silver	1,1-Dichloroethane	Benzo[g,h,i]perylene
Thallium	1,2-Dichloroethane	Benzo[k]Fluoranthene
Zinc	1,1-Dichloroethylene	Dibenzo[a,h]anthracene
	1,2-Dichloroethylene	Chrysene
	Ethylbenzene	Fluoranthene
Cyanide	Ethylene Dibromide	Fluorene
	Methylene Chloride	Indeno[1,2,3-cd]pyrene
	Methyl Ethyl Ketone	2-Methylnaphthalene
	Methyl t-Butyl Ether	Naphthalene
	Phenol	Phenanthrene
	PCBs	Pyrene
	Tetrachloroethylene	
	Toluene	
	1,1,1-Trichloroethane	
	Trichloroethylene	
	Vinyl Chloride	
	Xylenes	

6.1 Identification Of Extent Of Release Of OHM

The Phase II Comprehensive Site Investigation performed under the Massachusetts Contingency Plan is designed to gather sufficient data to define the extent of contamination at the disposal site. This data is collected in part to support the risk characterization process which is also required in Phase II. (For a discussion of data requirements for the development of Exposure Point Concentrations, see Section 8.6)

The data collected should be summarized in a manner which clearly indicates which oil or hazardous materials have been identified in each medium at the disposal site and in the surrounding environment. The most straightforward means of presenting such data is to construct a table (or set of tables) for each environmental medium. These tables would present summary statistics for each OHM, including the number of samples taken, the number of samples with concentrations reported above the Method Detection Limit, the arithmetic mean, standard deviation and the *range* of reported concentrations.

The raw data is often included as an appendix to the Phase II Report. The limit of detection should be included for each analysis. The limit of detection is the smallest concentration or amount of a substance that can be reliably detected by a given measurement process and distinguished from background noise. If the laboratory uses a different definition, that should also be reported. [Analytical results are often reported as "not-detected". Section 8.6.2.2 discusses how these values should be incorporated into the estimation of exposure point concentrations.]

Particular attention should be given to the adequacy of site sampling. Often times site sampling does not produce the data necessary to characterize exposures at a disposal site. The sampling plan should insure the collection of data which can adequately characterize exposures and risks at the disposal site, and the plan should be developed with input from the risk assessor. Exposure points and the activity patterns of potential receptors should be considered before the sampling is performed. A description or illustration of the sampling design (random, cluster, grid, stratified, etc.) should be included.

One of the most common shortcomings of Phase II Reports submitted to the Department is the inadequacy of the site data for use in the risk assessment. It is time- and cost-effective to consult with the risk assessor before the sampling plan is finalized.

The Department has issued a policy, *Suggested Outline, Content and Format of Phase II Human Health Risk Assessment Scope of Work*, (MA DEP, 1991b) which can assist the

site manager in identifying the data requirements of the risk assessment early in the site assessment process.

6.2 Elimination Of OHM From The Risk Assessment

The *Residential ShortForm* lists 49 individual chemicals for which risk may be characterized. The presence of a chemical on this list, however, does *not* imply that the risks associated with that chemical must *always* be estimated at *all* disposal sites. There are several reasons why an individual chemical may be dropped from the quantitative risk characterization, including:

- Reported levels are consistent with "background" and there is no evidence that their presence is related to the disposal at the location,
- Low frequency of detection and low concentration, and
- The chemicals are laboratory contaminants.

The first of these items is automatically addressed in the *Residential ShortForm*. The spreadsheet contains a screening mechanism which eliminates chemicals which are present at levels consistent with background. This background screen is discussed in more detail in Section 6.3, which follows.

If a chemical is reported in the analytic data at low frequency and low concentration, there are several options to evaluate. The risk assessor may determine that the existing data are insufficient and additional samples need to be taken to better describe the extent of contamination for that chemical. (The information may indicate the presence of a localized hot-spot.) If the data are considered to be sufficient to adequately characterize the disposal site, then the low concentration and frequency of detection may justify exclusion of the chemical from further quantitative risk assessment. In most such cases it is sufficient to discuss these contaminants qualitatively. It is the risk assessor's option, of course, to carry the chemical through the quantitative risk characterization, as this does not require much additional time or cost using the *ShortForm*.

Unfortunately it is not uncommon for an environmental sample to become contaminated with chemicals unrelated to the disposal site. Such contamination may occur in the field during the sample collection process, while the samples are being transported to the laboratory, or in the laboratory itself either during sample preparation or the actual analysis. The sampling plan should detail proper sampling and handling techniques, and include adequate **blank samples** to identify extraneous contamination should it occur.

Data which are determined to result from laboratory contamination may be excluded from the risk assessment.

The decision to eliminate chemicals from the quantitative risk assessment based on frequency of detection or laboratory contamination must be adequately justified with supporting data.

6.3 Comparison To Background Levels

The Massachusetts Contingency Plan requires that the background levels of oil or hazardous materials at the disposal site be identified (310 CMR 40.545(3)(e)). "Background" in the MCP is considered to be those levels of OHM which would exist in the absence of the disposal site. The identification of background levels, however, is often problematic due to technical considerations (care must be taken in the selection of sampling locations) and cost (each background sample translates into one less site sample). Background sampling is perceived to be pointless and contribute little to overall knowledge of the site. As a result, the temptation to use generic lists of background levels is very strong. Background information serves several purposes in the MCP risk management process, however, and the use of site-specific information may be very important in the determination of need for remediation and in the selection of a remedial alternative.

One use of the identified background levels is the selection of contaminants for exclusion from further assessment. Chemicals may be eliminated from the quantitative risk characterization if they are present at levels consistent with background. Local background information can be used in conjunction with the *ShortForm* in this manner, as described below.

For more generic application, the *Residential ShortForm* contains a background screening mechanism which will automatically compare the Exposure Point Concentrations entered by the risk assessor to a list of background concentrations contained in the spreadsheet (listed in the Toxicity Information table). There are two possible results:

- If the Exposure Point Concentration is less than the background concentration for that chemical, then the chemical is eliminated from further quantitative assessment and the notation "< Background" is inserted in the column for the Operational Exposure Point Concentration.

- If the EPC is equal to or greater than the background concentration for that chemical, then the Operational EPC is equal to the Exposure Point Concentration entered by the risk assessor.

The screening mechanism may be manually disabled by the risk assessor through the Options Menu in the *ShortForm*. Disabling the screen is useful when site-specific background levels are known and the risk assessor performs the background comparison manually. In this instance, the report generated would detail the identification of background levels, the comparison of Exposure Point Concentrations to these background levels, and any decisions to eliminate contaminants based upon the comparison. It may also be useful to disable the background screening mechanism when developing target cleanup levels and evaluating remedial alternatives.

There is not one concentration of a chemical, of course, which can correctly be labelled *the* background level. Hundreds of years of human activities have only broadened the naturally occurring range of concentrations reported as "background", and this range is best thought of as a statistical distribution. For the purposes of many environmental regulations, however, we often select point values from the range of representative background levels, and consider these to be representative of background. The use of such point-value "background" levels is essentially a short-cut method which allows consideration of background when little analytical data is available. When sufficient information has been collected (enough site-specific background and on-site samples to establish and describe distributions for each), comparisons to background can be accomplished through statistical tests of the sample populations. This is rarely the case, however, and the *Residential ShortForm* has incorporated the short-cut method using a point value for its background comparisons.

The point values selected for the *ShortForm* background comparisons have been chosen so that the majority of chemicals which are present at concentrations consistent with background would be dropped from further quantitative risk assessment. Given the wide ranges seen in distributions of background concentrations it is clear that the choice of a point value within that range balances the need to eliminate background chemicals with the need to retain for evaluation those chemicals whose presence is related to the disposal practices at the site but which are reported at relatively low to moderate concentrations. [The terms "low" to "moderate" are used here in a subjective sense to describe concentrations which may be in or slightly above the upper bounds of the background range. The terms imply nothing about potential human health risks.] It is inevitable that some chemicals which are unrelated to the site disposal but present at concentrations at the high end of the background range will not be caught by the *ShortForm's* background screen. Conversely, some chemicals which *are* related to the

disposal practices at the site (and are not background) will be screened out of the risk assessment by the *ShortForm*. The goal is to minimize both kinds of error.

The *Residential ShortForm* does not contain background concentrations for all chemicals in all media, although the Department is continuing work in this area. Until such values are identified, any reported concentration for a chemical lacking a background level is assumed to be above background and the associated risks will be calculated. Alternatively, the risk assessor may identify medium-specific background concentrations for the chemical and perform the background screen manually. The documentation for the identification of the background value and the manual background screen should be included in the written report.

The following sections describe the background values identified for use in the *Residential ShortForm*. The background concentrations were selected from several different data sources as no one source was determined to be adequate. General factors which influenced the selection of these values included the size of the data set from which they were derived, their suitability for comparison to Massachusetts environmental media and their comparability to analytical data typically generated at 21E disposal sites.

6.3.1 Background Levels In Soil

Soil background levels have been identified for 24 chemicals and a list of these values is given in Table 6-2. These soil background levels are described in the sections which follow, grouped according to the data sets from which they were derived.

6.3.1.1 Chromium, Lead, Nickel and Zinc

The background soil concentrations for these four chemicals were estimated from a data set published by Peter Veneman of the Department of Plant and Soil Sciences at the University of Massachusetts at Amherst (Veneman, 1985). This data set consists of individual data points for various locations throughout Massachusetts. The Veneman data were preferred when available because it is a large data set, it represents only Massachusetts conditions, and the sampling and analysis were done in a manner that appeared to be both more consistent from location to location and more comparable with methods used in site assessment.

The data selected consisted of 36 surficial (approximately 0-2 feet) soil samples. Samples taken from current or former orchards were excised from the lead data set, however, due to historic pesticide use. This left 28 data points for lead.

For each of the four chemicals, cumulative frequency plots were generated for each chemical (Figures 6-1 through 6-4) and the 95th Percentile value was estimated graphically.

Table 6-2

SHORTFORM SOIL BACKGROUND CONCENTRATIONS			
Chemical	Background Soil Conc. mg/kg	Chemical	Background Soil Conc. mg/kg
Arsenic	32	Fluoranthene	0.5
Acenaphthene	0.5	Fluorene	0.5
Acenaphthylene	0.5	Indeno[1,2,3-cd]pyrene	0.5
Anthracene	0.5	Lead	69
Benzo[a]anthracene	0.5	Mercury	0.5
Benzo[a]pyrene	0.5	2-Methylnaphthalene	0.5
Benzo[b]fluoranthene	0.5	Naphthalene	0.5
Benzo[g,h,i]perylene	0.5	Nickel	30
Benzo[k]fluoranthene	0.5	Phenanthrene	0.5
Chromium	105	Pyrene	0.5
Chrysene	0.5	Thallium	19
Dibenzo[a,h]anthracene	0.5	Zinc	110

6.3.1.2 Arsenic and Mercury

The background concentrations for these two chemicals are taken from the U.S. Geological Services Professional Paper 1270 (Shacklette, 1984). This report summarized data rather than list the individual data points. For each chemical, the number of samples, range, geometric mean and deviation were given. Assuming that each data set fit a lognormal distribution, the upper 95th Percent limit was estimated as described in Table 6-3. The 95th limit (corresponding approximately to the 97.5th percentile value) was chosen as the concentration below which background concentrations of arsenic and mercury are likely to fall at most locations. Table 6-3 presents this information for these chemicals.

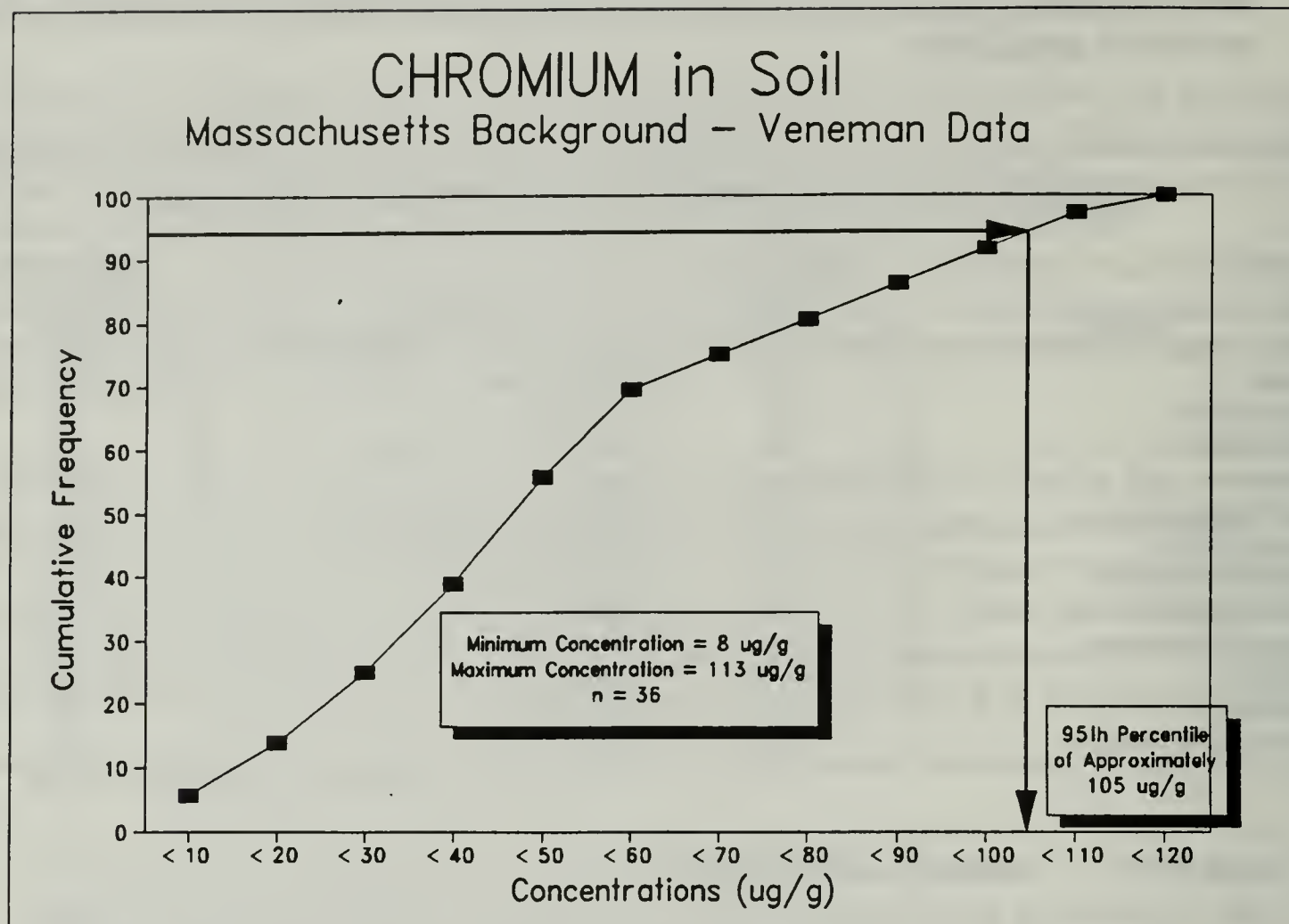


Figure 6-1

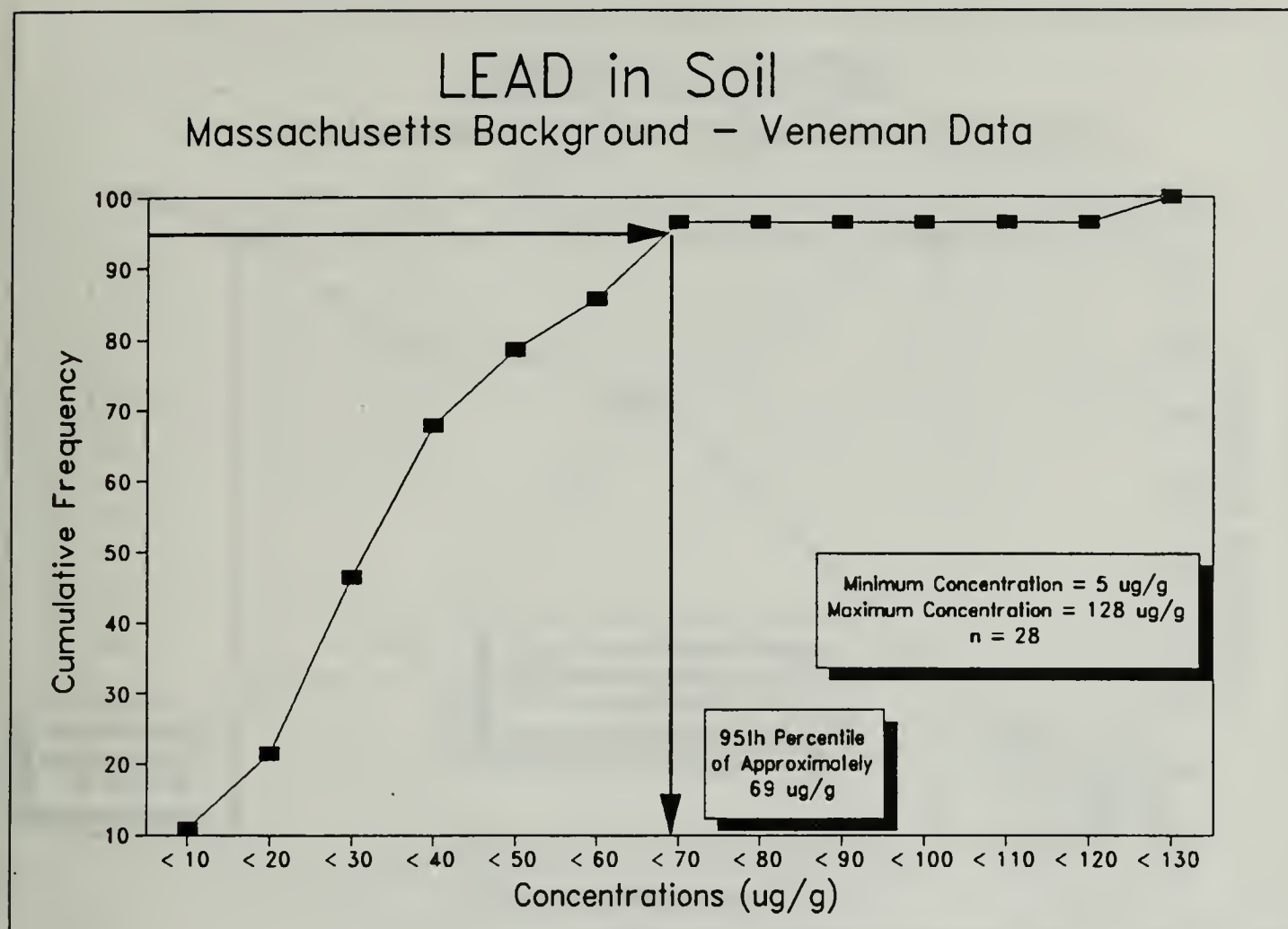


Figure 6-2

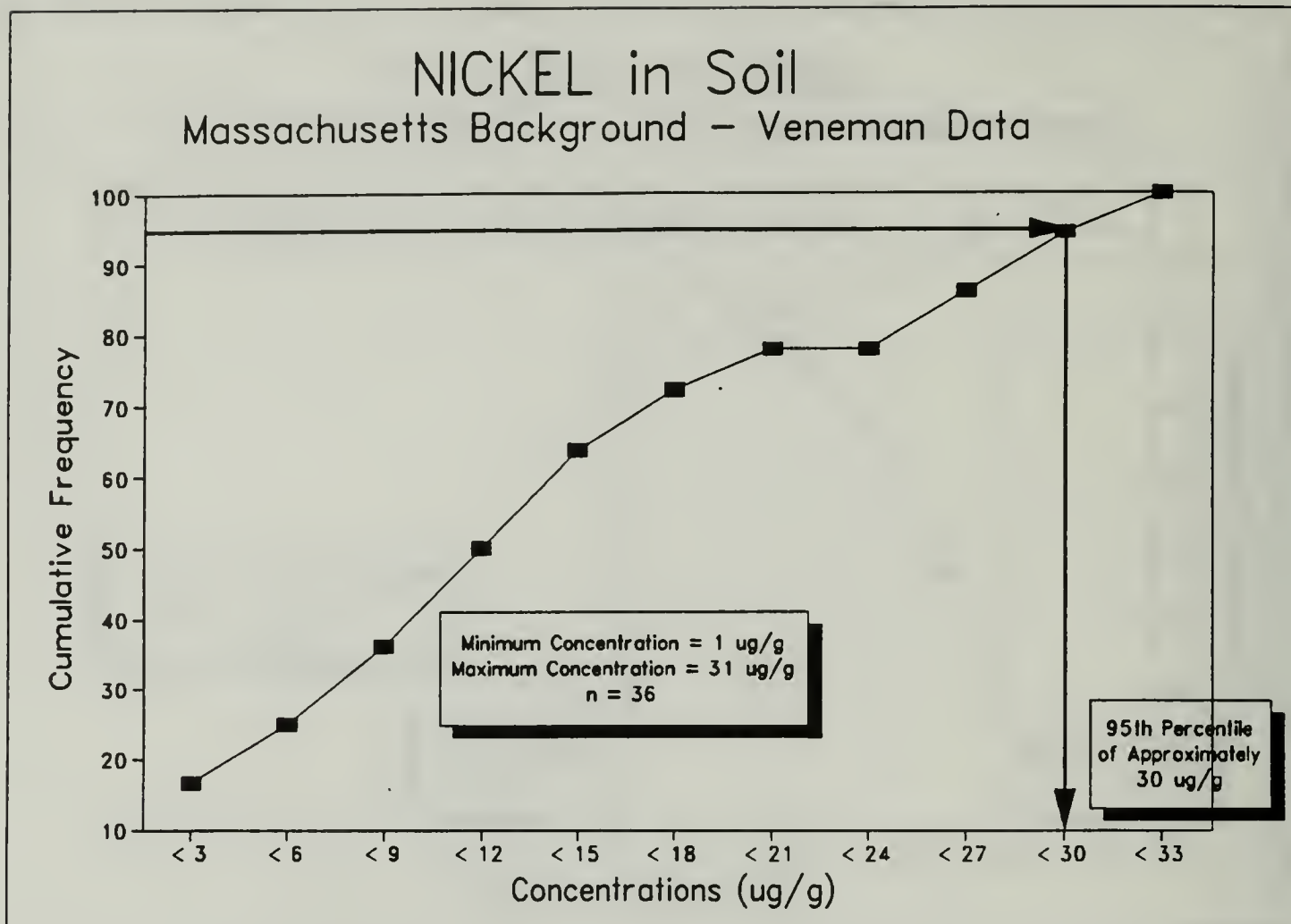


Figure 6-3

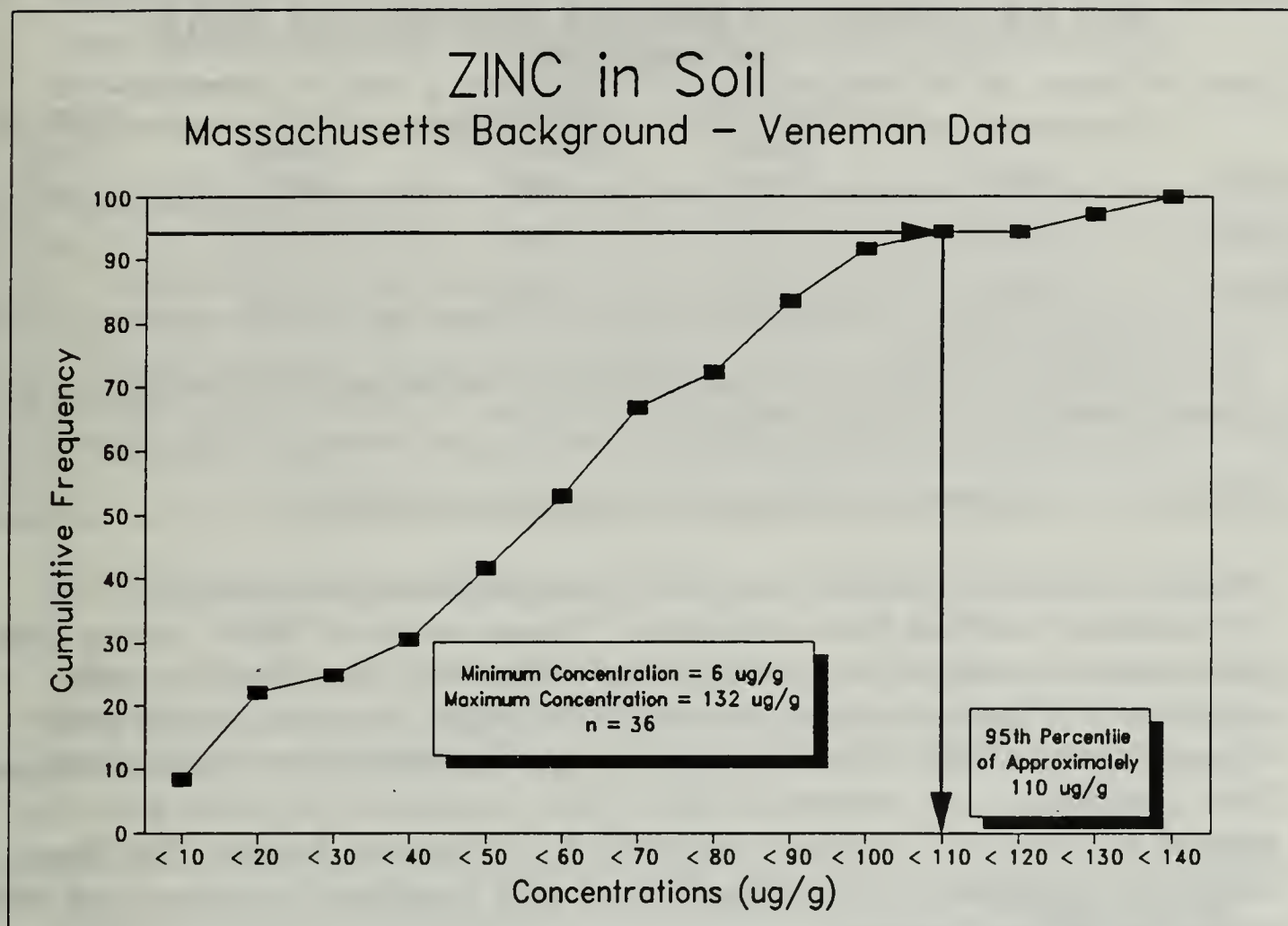


Figure 6-4

TABLE 6-3

METALS CONCENTRATIONS IN EASTERN U.S. SOILS					
from Shacklette, 1984)					
METAL	RATIO ^a	GEOMETRIC MEAN ($\mu\text{g/g}$)	GEOMETRIC DEVIATION ($\mu\text{g/g}$)	RANGE ($\mu\text{g/g}$)	UPPER 95% LIMIT ^b ($\mu\text{g/g}$)
Arsenic	521/527	4.8	2.56	<0.1 - 73	32
Mercury	534/534	0.081	2.52	0.01 - 3.4	0.5
^a - Ratio = # detected/# Samples ^b - 95% of the samples in randomly selected soil should fall between the levels $M \times D^2$ and M/D^2 , where M is the geometric mean and D is the geometric deviation.					

6.3.1.3 Polycyclic Aromatic Hydrocarbons (PAHs)

Polycyclic Aromatic Hydrocarbons (PAHs) are ubiquitous environmental contaminants resulting from combustion. Known sources of PAHs include forest fires, waste incineration, and the burning of fossil fuels in automobiles and airplanes. PAHs are often reported at C.21E disposal sites, and "background" values (listed in Table 6-2) are included in the *Residential ShortForm* to eliminate from quantitative risk assessment those PAHs consistent with levels from the general anthropogenic non-point sources. *It is recognized, however, that these values do not represent clear delineations of what situations are and are not related to discrete disposal sources.*

A review of the literature (Edwards, 1983; Jones, 1989a and 1989b; Vogt, 1987; Youngblood, 1975; and Wang, 1981) and MA DEP data (MA DEQE, 1989b; MA DEP, 1990b) provided a range of Total PAH values from 0.073 ppm (mean) to 60.3 ppm (one sample) from areas considered to be background (in this case, background is considered to be an area not associated with a known point-source. It is not necessarily pristine.) Based on this information, a Total PAH level of 10 ppm has been identified as an upper percentile value "background" concentration. This Total value has been apportioned among the 17 PAH compounds listed in the *Residential ShortForm*, resulting in a value of approximately 0.5 ppm for each compound.

The apportioned value of 0.5 ppm for each of the *Residential ShortForm* PAHs may not be appropriate in situations where only one of two PAHs are present. The user is reminded that site-specific information can be used to screen contaminants of concern *before* Exposure Point Concentrations are entered into the spreadsheet (Section 6.3). Alternatively, the concentration of Total PAHs may

be *manually* compared to the 10 ppm Total PAH level discussed above. Exposure Point Concentrations would not be entered into the *ShortForm* if the calculated Total PAH concentration were *less than* the 10 ppm "background" level. Documentation of such a comparison must be included in the report to justify the elimination of PAH compounds from further quantitative assessment.

The Department is extremely wary of the publication of these values, and the risk assessor is cautioned against using them in any other context. Further research is necessary to better identify "background" levels for each of the PAH compounds, and these values are sure to be updated in later versions of the *ShortForm*.

6.3.2 Background Levels In Air

Indoor air background levels have been identified for 13 chemicals and a list of these values is given in Table 6-4. These levels are described in the sections which follow, grouped according to the source from which they were taken.

TABLE 6-4

SHORTFORM INDOOR AIR BACKGROUND CONCENTRATIONS			
Chemical	Background Indoor Air Conc. $\mu\text{g}/\text{m}^3$	Chemical	Background Indoor Air Conc. $\mu\text{g}/\text{m}^3$
Benzene	21	Naphthalene	5
Carbon Tetrachloride	1	Tetrachloroethylene	11
Chlorobenzene	10	Toluene	29
Chloroform	3	1,1,1-Trichloroethane	30
Ethylbenzene	10	Trichloroethylene	5
Methylene Chloride	600	Xylenes	40
Methyl Ethyl Ketone	42		

6.3.2.1 Benzene, Carbon Tetrachloride, Chloroform, Ethylbenzene, Methyl Ethyl Ketone, Tetrachloroethylene, Toluene, 1,1,1-Trichloroethane, Trichloroethylene

The background concentrations in indoor air for these nine chemicals were taken from an analysis of the National Ambient Volatile Organic Compounds Data Base (Shah, 1988). The concentrations chosen from this database represent the Upper Quartile (75%) values from each of the data sets. Table 6-5 presents these data. This data base was chosen as the principal source for the indoor air background concentrations, due primarily to the large number of samples, on the order of approximately 2000 per chemical (Methyl Ethyl Ketone and Toluene being the exceptions with 4 and 220 samples respectively).

The values were presented in the paper in parts-per-billion by volume, and were converted to $\mu\text{g}/\text{m}^3$ for use in the *ShortForm*: $\mu\text{g}/\text{m}^3 = (\text{ppbv} * \text{MW}) \div 24.45$ (@ 25° C), where MW is the compound's molecular weight.

TABLE 6-5

INDOOR AIR CONCENTRATIONS				
(modified from Shah, 1988)				
Chemical	# of Data Points	Average $\mu\text{g}/\text{m}^3$	Median $\mu\text{g}/\text{m}^3$	Upper Quartile $\mu\text{g}/\text{m}^3$
Benzene	2128	16.5	10	21
Carbon Tetrachloride	2120	2.5	0.0	0.8
Chloroform	2120	4.0	0.51	3.4
Ethylbenzene	2278	12.5	4.8	9.6
Methyl Ethyl Ketone	4	27.2	21.1	42.2
Tetrachloroethylene	2195	20.7	5.0	11.0
Toluene	220	27.8	6.2	28.7
1,1,1-Trichloroethane	2120	266	10	29.9
Trichloroethylene	2132	7.3	0.7	4.6

6.3.2.2 Chlorobenzene, Methylene Chloride, Xylenes, Naphthalene

The background concentrations in indoor air for these four chemicals were taken from an analysis of VOCs in the residential environment (Stolwijk, 1990). This paper presents the arithmetic mean and 10th, 50th, 90th, and 98th percentile values for various organic compounds in indoor air, generated primarily from a German survey of 500 homes, but considering additional studies yielding a total of 1160 homes sampled. The author notes that the figures presented have a range of uncertainty of about 50%.

Table 6-6 presents the indoor air concentrations for these four chemicals. The 90th percentile value was chosen for use in the *ShortForm* for the background comparison screen. The values were presented in $\mu\text{g}/\text{m}^3$, and needed no further conversion.

TABLE 6-6

INDOOR AIR CONCENTRATIONS (from Stolwijk, 1990)			
Chemical	Arithmetic Mean, $\mu\text{g}/\text{m}^3$	50 th Percentile $\mu\text{g}/\text{m}^3$	90 th Percentile $\mu\text{g}/\text{m}^3$
Chlorobenzene	1	< 0.5	10
Methylene Chloride	NC ^a	< 10	600
Naphthalene	NC	2	5
<i>m,p</i> -Xylenes	20	20	40 ^b
<i>o</i> -Xylene	10	5	10
^a NC = Not Calculated ^b The 90 th percentile value for the <i>m,p</i> -Xylenes was chosen as the background concentration for <i>Total Xylenes</i> in the absence of such a value for <i>Total</i> .			

6.3.3 Background Levels In Groundwater

Groundwater background levels have been identified for six metals and a list of these values is given in Table 6-7. These concentrations were developed from a data set collected by the Massachusetts DEP Division of Water Supply and computerized by volunteers from the Streamlining Risk Assessment Workgroup.

The MA DEP Division of Water Supply (DWS) has been collecting routine drinking water samples from public water supplies for over 15 years. Analytical results from this sampling program have been kept according to town name in DWS files. The analyses were carried out primarily by the MA DEP's Lawrence Experiment Station. As the data included both surface and groundwater sources, only those samples specifically described as coming from a well were selected. A total of 114 well samples were identified, although results were not reported for all chemicals in all samples. Thus the number of samples (n) for any given chemical actually varies from 49 to 73.

Table 6-7

SHORTFORM GROUNDWATER BACKGROUND CONCENTRATIONS (from MA DEP DWS Data)			
Chemical	Background Groundwater Concentr. µg/L	Chemical	Background Groundwater Concentr. µg/L
Arsenic	5.5	Lead	8.8
Cadmium	4.2	Mercury	0.95
Chromium	4.9	Silver	4.7

In the analysis of this data, results reported as being less than a detection limit were automatically assigned a value equal to $\frac{1}{2}$ the limit of detection. It was not uncommon to find variation up to an order of magnitude in the detection limits for any given chemical.

Table 6-8 presents the number of samples, the arithmetic mean, 50th percentile and 95th percentile values for each chemical listed in the *ShortForm* for which data was found in the DWS files.

Table 6-8

METALS CONCENTRATIONS IN MASSACHUSETTS GROUNDWATERS (from MA DEP DWS Data)					
CHEMICAL	# of Data Points (n)	% of Samples < DL	Arithmetic Mean µg/L	50 th Percentile µg/L	95 th Percentile µg/L
Arsenic	70	57	4.4	1.5	5.5
Cadmium	55	87	3.2	0.5	4.2
Chromium	73	66	2.1	1	4.9
Lead	64	48	4.8	2	8.8
Mercury	60	73	0.36	0.1	0.95
Silver	49	98	0.9	0.5	4.7

6.4 Toxicity Profiles

Toxicity Profiles or Summaries are provided in Appendix B for each of the chemicals (or groups of chemicals) included in the *Residential ShortForm*.

Toxicity Profiles serve several purposes. First, they are summaries of the potential human health hazards posed by each OHM, and include references for the dose-response relationships described in Section 7.0 of this document. The Toxicity Profiles included with the *ShortForm* contain six sections:

- General Background Information
- Pharmacokinetics
- Human Toxicological Profile
- Mammalian Toxicological Profile
- Genotoxicity
- References

Information contained in the Toxicity Profiles may be used to group chemicals by health endpoint and mechanism of toxicity in order to estimate more detailed Hazard Indices (Sections 9.0 and 10.0).

The profiles also serve as accessible reference material for non-toxicologists affiliated with the site, including site owners, site managers, DEP staff and the general public who are concerned about the potential health impacts associated with the contaminants found at the site. As part of the Hazard Identification component of the risk assessment, these toxicity profiles should be copied and included in the Phase II Report.

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7.0 DOSE RESPONSE ASSESSMENT

7.1 Basic Assumptions

In general, the dose-response assessment describes the observed effects in humans and/or laboratory animals associated with particular exposures (or doses) of the chemical of concern. This information is obtained from published literature describing epidemiologic or toxicologic studies involving the particular chemical.

The TOXICITY INFORMATION section of the *ShortForm* contains the dose-response information for each of the OHM listed in the spreadsheet. This information is later coupled with information on the nature and magnitude of the hypothetical residential exposures in order to characterize risk.

The dose-response information contained in the *ShortForm* may be divided into three major categories:

- Toxicity information associated with threshold (non-carcinogenic) health effects.
- Toxicity information concerning carcinogenicity, either from human epidemiologic data or from laboratory studies.
- The Relative Absorption Factors (RAFs) used to relate the toxicity values from the literature to the exposure pathways of concern in this spreadsheet.

All the chemicals listed in the *Residential ShortForm* are evaluated for potential *non-carcinogenic* health effects. In addition, any substance considered to be a *known*, *probable*, or *possible* human carcinogen is also evaluated for its potential carcinogenic effect. The classification of a chemical as a carcinogen does not preclude an evaluation of that same chemical for potential non-carcinogenic health risks.

7.1.1 Threshold Effects

For non-carcinogenic health effects it is believed that a dose level exists at and below which no adverse health effects would be expected. Such a level is referred to as a *threshold dose*. While it is impossible to specify a theoretical threshold dose for a given chemical, it is possible to estimate a human sub-threshold dose at which no adverse health effects would be expected. Such a value is typically derived from the No Observable Adverse Effects Level (NOAEL) of an animal study by application of uncertainty factors (UF) to account for interspecies variation, exposure duration and to protect sensitive populations. Important factors to consider when identifying and using such a sub-threshold dose include:

- the route of administration of the dose (inhalation, oral, dermal contact, etc...)
- the duration of exposure to that dose (lifetime, chronic, subchronic, or acute exposure)
- the absorption efficiency (if any) used to calculate that dose
- the age of the person receiving the dose.

7.1.2 Carcinogenic Effects

Unlike the non-carcinogenic health effects, it is generally assumed that there is no threshold dose for carcinogenicity, that there is no dose of a carcinogenic substance (other than no exposure) which is associated with zero risk. The ability of a chemical to increase the incidence of cancer in a target population is described by one of two measures: the *carcinogenic potency value* or the *unit risk*. These values are listed in the *Residential ShortForm* in the TOXICITY INFORMATION section for any chemical considered to be carcinogenic.

7.1.2.1 Carcinogenic Potency Value (CPV)

The Carcinogenic Potency (or Slope) Value for a chemical is derived by the EPA's Cancer Assessment Group (CAG). Using data derived from animal studies, the Potency Value is an estimate of the upper 95% Confidence Limit of the slope of the dose-response curve extrapolated to low doses. For some chemicals, human epidemiologic data is the basis of an estimate of the carcinogenic potency, although the most common basis of these values is an animal study.

The Potency value is given in units of $(\text{mg/kg/day})^{-1}$. It is based upon the concept of a lifetime average daily dose. While both oral and inhalation potency values

have been developed, the *Residential ShortForm* uses only the oral CPVs to evaluate oral and dermal exposures.

7.1.2.2 Inhalation Unit Risk Values (URs)

The Inhalation Unit Risk is the upper 95% Confidence Limit of the mean incremental lifetime cancer risk estimated to result from lifetime exposure to an agent if it is in the air at a concentration of $1 \mu\text{g}/\text{m}^3$ or in the drinking water at a concentration of $1 \mu\text{g}/\text{L}$. These values are used in lieu of the chemical's Potency Value when an estimate of a lifetime average concentration of the chemical is available. The *Residential ShortForm* uses the unit risk in air to evaluate inhalation exposures.

7.1.3 Relative Absorption Factors (RAFs)

The equations used in the *Residential ShortForm* incorporate Relative Absorption Factors (RAFs) which have been determined or estimated for each chemical via each route of exposure.

The RAF addresses two major issues:

- the absorption efficiency for the chemical via the route and medium of exposure being evaluated for the disposal site, and
- the absorption efficiency for the route and medium of exposure in the experimental study which is the basis of the Reference Dose or the Potency Value for the chemical in question.

Thus the RAF adjusts the dose (or exposure) estimates based on these *two* absorption efficiencies. MA DEQE (1989a) describes the development of RAFs in its Appendix B. (The factors were called "*Bioavailability Adjustment Factors*", or "*BAFs*" in that document.) US EPA (1989a), Appendix A also provides guidance for the "*Adjustments For Absorption Efficiency*".

The risk assessor is reminded that an absorption efficiency (or absorption factor) which doesn't consider derivation of the toxicity values (Reference Dose, Reference Concentration, Potency Value or Unit Risk) is not an RAF.

The RAFs used in the *Residential ShortForm* calculations are listed in the TOXICITY INFORMATION section of the spreadsheet, and the derivation of individual RAF values is described in APPENDIX C.

7.2 Sources of Dose-Response Information

7.2.1 Threshold Effects

Several types of "sub-threshold dose" values have been identified or developed for use in *ShortForm*. The sources of these values are described in general below. The TOXICITY INFORMATION section of the *Residential ShortForm* is reproduced in Table 7-1. The source for a specific toxicity value may be found using the references adjacent to each value in the table, and the list of references at the end of Table 7-1.

7.2.1.1 Oral and Dermal Exposures

The U.S. EPA derived oral Reference Dose (RfD) is used in the *Residential ShortForm* when one is available for the chemical of concern. Chronic RfDs are available from the U.S. EPA's on-line database, the *Integrated Risk Information System* (IRIS). Subchronic RfDs from the U.S. EPA's *Health Effects Assessment Summary Tables* (HEAST) are used for the evaluation of subchronic exposures. HEAST also serves as a source of US EPA derived chronic RfDs.

When a subchronic or chronic RfD is not available from IRIS or HEAST for a chemical in the *ShortForm*, an analogous toxicity value has been identified or developed by MA DEP Office of Research and Standards staff. The documentation for these values is provided in APPENDIX D.

7.2.1.2 Inhalation Exposures

The U.S. EPA derived inhalation Reference Concentration (RfC) is used in the *Residential ShortForm* when one is available for the chemical of concern. Chronic RfCs are available from the U.S. EPA's IRIS (as the primary source) and HEAST. Subchronic RfCs from HEAST are used for the evaluation of subchronic exposures.

In the absence of an EPA derived Reference Concentration, the "Allowable Threshold Concentration" (MA DEQE, 1989a) is used. The Allowable Threshold Concentration (ATC) is a value derived from the Threshold Effects Exposure Limit (TEL) described in CHEM (MA DEP, 1990c). (The TEL value represents 20% of an allowable concentration, or ATC. Thus the ATC is equal to five times the TEL. The TEL was derived in a manner considering children to be the most sensitive potential receptors.) The ATC is a concentration of the chemical in air which would not be expected to result in adverse non-carcinogenic health effects. The

ATC is derived considering acute and chronic threshold health endpoints, including reproductive effects.

When neither an RfC nor ATC is available for a chemical listed in the *ShortForm*, MA DEP Office of Research and Standards staff has identified or developed an analogous toxicity value. The documentation for these values is provided in APPENDIX D.

7.2.2 Carcinogenic Effects

7.2.2.1 Oral and Dermal Exposures

The U.S. EPA derived oral Carcinogenic Potency Value (CPV) is used to evaluate both oral and dermal exposure to carcinogens. The U.S. EPA's *IRIS* database and the *Health Effects Assessment Summary Tables* serve as the primary and secondary sources of the potency values.

7.2.2.2 Inhalation Exposure

When available, the U.S. EPA derived Unit Risk (UR) is used to evaluate indoor air exposures in the *ShortForm*. Again, *IRIS* and *HEAST* serve as the sources of these unit risk values. *CHEM* (MA DEP, 1990c) is used as a secondary source for these values.

7.2.3 Relative Absorption Factors

Currently there are no published lists of Relative Absorption Factors (RAFs) derived in a manner consistent with Massachusetts or Federal guidance (MA DEQE 1989a; US EPA 1989a). The RAFs listed in the TOXICITY INFORMATION section of the spreadsheet were developed specifically for the *ShortForm* by MA DEP Office of Research and Standards staff. The documentation for the development of the RAFs is contained in APPENDIX C.

As new toxicity values are constantly being proposed and old values updated, it is important that each toxicity value be adequately referenced and that the most recent values be used. *At a minimum*, the *Residential ShortForm* will be updated annually (in September) to insure that the toxicity values contained in the spreadsheet remain current. More frequent updates may also occur as considered necessary, and the user is urged to add their name and address to the Department's mailing list (see page ii) and to constantly check the MA DEP/ORS computer bulletin board for relevant announcements.

7.3 Toxicity Information Summary Tables

The following summary tables are extracted from the *Residential ShortForm* and reproduced here to document the selection and development of individual toxicity values. The numerical references contained in Table 7-1 are explained at the end of that table.

TABLE 7-1
SHORTFORM TOXICITY VALUES
(TABLES FROM THE SHORTFORM)

TOXICITY INFORMATION

TOXICITY INFORMATION	SUBCHRONIC REF	CHRONIC REF	REF	CHRONIC INHALATION REFERENCE CONC	REF	CLASS,	REF	INHALATION CANCER UNIT RISK	CLASS, REF	DERMAL CANCER POTENCY FACTOR	REF	RAF SC SOIL INGEST
(OR SUBSTITUTED) mg/kg/day	(OR SUBSTITUTED) mg/kg/day	(OR SUBSTITUTED) mg/kg/day	(OR SUBSTITUTED) mg/kg/day	(OR SUBSTITUTED) ug/cu m	(OR SUBSTITUTED) ug/cu m			1/(ug/cu m)		1/(mg/kg/day)		1/(mg/kg/day)
OIL OR HAZARDOUS MATERIAL												
ARSENIC	3.0E-04	2	3.0E-04	1	NOT VOLATILE	NOT VOLATILE	1.8E+00	1.8E+00	1a	1	1	1
CADMIUM	1.0E-03	2e	1.0E-03	2d	NOT VOLATILE	NOT VOLATILE	ND	1	NOT VOLATILE	1	1	1
CHROMIUM	2.0E-02	2g	5.0E-03	1d	NOT VOLATILE	NOT VOLATILE	B2	1	NOT VOLATILE	1	1	1
LEAD	7.5E-04	4	7.5E-04	4	NOT VOLATILE	NOT VOLATILE	D	1	NOT VOLATILE	1	0.5	1
MERCURY	3.0E-04	2	3.0E-04	2	3.0E-01	2	D	1	NOT VOLATILE	1	1	1
NICKEL	2.0E-02	2	2.0E-02	1	NOT VOLATILE	NOT VOLATILE	D	1	NOT VOLATILE	1	1	1
SILVER	5.0E-03	2	5.0E-03	1	NOT VOLATILE	NOT VOLATILE	D	1	NOT VOLATILE	1	1	1
THALLIUM	7.0E-04	2	7.0E-05	2	NOT VOLATILE	NOT VOLATILE	D	1	NOT VOLATILE	1	1	1
ZINC	2.0E-01	2	2.0E-01	2	NOT VOLATILE	NOT VOLATILE	D	1	NOT VOLATILE	1	1	1
BENZENE	5.0E-02	4	5.0E-03	4	3.2E+01	4	A	1	8.3E-06	A	1	1
Bis(2-ethylhexyl)PHTHALAT	2.0E-02	2	2.0E-02	1	NOT VOLATILE	NOT VOLATILE	B2	1	NOT VOLATILE	1.4E-02	1a	1
CARBON TETRACHLORIDE	7.0E-03	2	7.0E-04	1	4.3E+02	3a	B2	1	1.5E-05	B2	1	1
CHLOROBENZENE	2.0E-01	2	2.0E-02	1	2.0E+02	2	D	1	2.3E-05	B2	1	1
CHLOROFORM	1.0E-02	2	1.0E-02	1	6.6E+02	3a	B2	1	2.3E-05	B2	1	1
1,1-DICHLOROETHANE	1.0E+00	2	1.0E-01	2	5.0E+02	2	C	2	2.6E-05	B2	2	1.3
1,2-DICHLOROETHANE	2.0E-01	4	2.0E-02	4	5.5E+01	3a	B2	2	2.6E-05	B2	2	1
1,1-DICHLOROETHYLENE	9.0E-03	2	9.0E-03	1	5.0E+00	3a	C	1	5.0E-05	C	1	1
1,2-DICHLOROETHYLENE	2.0E-01	2	2.0E-02	1	1.1E+03	3a	D	1	2.2E-04	B2	1	1
ETHYLBENZENE	1.0E+00	2	1.0E-01	1	1.0E+03	2	B2	1	4.7E-07	B2	1	1
ETHYLENE DIBROMIDE	2.0E-04	4	2.0E-05	4	1.2E+00	4	B2	1	8.5E+01	1a	1	1
METHYLENE CHLORIDE	6.0E-02	2	6.0E-02	1	3.0E+03	2	B2	1	7.5E-03	1a	1	1
METHYL ETHYL KETONE	5.0E-01	2	5.0E-02	2	3.0E+03	2	D	1	NOT VOLATILE	NOT VOLATILE	1	1
METYL TERT BUTYL ETHER	5.2E-02	4	5.2E-03	4	5.0E+02	1c	D	1	NOT VOLATILE	NOT VOLATILE	1	1
PHENOL	6.0E-01	2	6.0E-01	1	NOT VOLATILE	NOT VOLATILE	D	1	NOT VOLATILE	NOT VOLATILE	1	1
PCB	5.0E-06	4	5.0E-06	4	NOT VOLATILE	NOT VOLATILE	B2	1	NOT VOLATILE	NOT VOLATILE	1	0.85
TETRACHLOROETHYLENE	1.0E-01	2	1.0E-02	1	4.6E+03	3a	C-B2	2h	5.8E-07	C-B2	2h	1
TOLUENE	2.0E+00	2	2.0E-01	1	2.0E+03	2	D	1	5.8E-07	C-B2	2h	1
1,1,1-TRICHLOROETHANE	9.0E-01	2	9.0E-02	2	1.0E+04	2	D	1	5.8E-07	C-B2	2h	1
TRICHLOROETHYLENE	2.0E-02	4	2.0E-03	4	1.8E+02	3a	C-B2	2h	1.7E-06	C-B2	2h	1
VINYL CHLORIDE	1.0E-03	4	1.0E-03	4	1.7E+01	3a	A	2	8.4E-05	A	2	1
XYLENES	4.0E+00	2	2.0E+00	1	3.0E+02	2	D	1	1.9E+00	2a	1	1
CYANIDE	2.0E-02	2	2.0E-02	1	1.0E+00	4	D	1	NOT VOLATILE	NOT VOLATILE	1	1

TOXICITY INFORMATION

TOXICITY INFORMATION	SUBCHRONIC ORAL REFERENCE DOSE (OR SUBSTITUTE) mg/kg/day	REF	CHRONIC ORAL REFERENCE DOSE (OR SUBSTITUTE) mg/kg/day	REF	SUBCHRONIC INHALATION REFERENCE CONC (OR SUBSTITUTE) ug/cu m	REF	CHRONIC INHALATION REFERENCE CONC (OR SUBSTITUTE) ug/cu m	REF	CLASS, CANCER	REF	INHALATION CANCER UNIT RISK 1/(ug/cu m)	CLASS, REF	DERMAL CANCER POTENCY FACTOR 1/(mg/kg/day)	REF	RAF SC SOIL INGEST
OIL OR HAZARDOUS MATERIAL															
PAHs(LISTED BELOW)															
ACENAPHTHENE	6.0E-01	2	6.0E-02	1	NOT VOLATILE		NOT VOLATILE		D	1	NOT VOLATILE			1	
ACENAPHTHYLENE	4.0E-02	2b	4.0E-02	2f	NOT VOLATILE		NOT VOLATILE		D	1	NOT VOLATILE			0.91	
ANTHRACENE	3.0E+00	2	3.0E-01	1	NOT VOLATILE		NOT VOLATILE		B2	1g	NOT VOLATILE		7.3E+00	1a	
BENZO(a)ANTHRACENE	4.0E-02	2b	4.0E-02	2f	NOT VOLATILE		NOT VOLATILE		B2	1g	NOT VOLATILE		7.3E+00	1a	
DIBENZO(a,h)ANTHRACENE	4.0E-02	2b	4.0E-02	2f	NOT VOLATILE		NOT VOLATILE		B2	1	NOT VOLATILE		7.3E+00	1a	
BENZO(a)PYRENE	4.0E-02	2b	4.0E-02	2f	NOT VOLATILE		NOT VOLATILE		B2	1g	NOT VOLATILE		7.3E+00	1a	
BENZO(b)FLUORANTHENE	4.0E-02	2b	4.0E-02	2f	NOT VOLATILE		NOT VOLATILE		B2	1g	NOT VOLATILE		7.3E+00	1a	
BENZO(g,h,i)PERYLENE	4.0E-02	2b	4.0E-02	2f	NOT VOLATILE		NOT VOLATILE		B2	1g	NOT VOLATILE		7.3E+00	1a	
BENZO(k)FLUORANTHENE	4.0E-02	2b	4.0E-02	2f	NOT VOLATILE		NOT VOLATILE		B2	1g	NOT VOLATILE		7.3E+00	1a	
CHRYSENE	4.0E-01	2	4.0E-02	1	NOT VOLATILE		NOT VOLATILE		B2	1g	NOT VOLATILE		7.3E+00	1a	
FLUORANTHENE	4.0E-01	2	4.0E-02	1	NOT VOLATILE		NOT VOLATILE		B2	1g	NOT VOLATILE		7.3E+00	1a	
INDENO(1,2,3-cd)PYRENE	4.0E-02	2b	4.0E-02	2f	NOT VOLATILE	3a	NOT VOLATILE	3b	B2	1g	NOT VOLATILE		7.3E+00	1a	
2-METHYLNAPHTHALENE	4.0E-02	2b	4.0E-02	2f	7.1E+01	3a	7.1E+01	3b	D	1	D	1			
NAPHTHALENE	4.0E-02	2	4.0E-02	2f	NOT VOLATILE		NOT VOLATILE		D	1	NOT VOLATILE				
PHENANTHRENE	4.0E-02	2b	4.0E-02	2f	NOT VOLATILE		NOT VOLATILE		D	1	NOT VOLATILE				
PYRENE	3.0E-01	2	3.0E-02	1	NOT VOLATILE		NOT VOLATILE		D	1	NOT VOLATILE				

TOXICITY INFORMATION

TOXICITY INFORMATION

OIL OR HAZARDOUS MATERIAL

	0.03	1	0.03	1	0.03	1	1	1	1	1	1	1	1	1	1	1	1	1	32	5.5	7.1E-08	3.0E-07	2.6E-07
ARSENIC	0.03	1	0.03	1	0.03	1	1	1	1	1	1	1	1	1	1	1	1	1	32	5.5	7.1E-08	3.0E-07	2.6E-07
CADMIUM	0.14	1	0.14	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	105	4.2	5.0E-06	4.4E-06	5.0E-06
CHROMIUM	0.09	1	0.09	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	105	4.9	9.2E-06	6.8E-06	9.2E-06
LEAD	0.006	0.5	0.006	1	NC	NC	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	69	8.8	3.8E-07	3.4E-07	3.8E-07	
MERCURY	0.05	1	0.05	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	1	0.95	5.0E-07	4.5E-07	5.0E-07
NICKEL	0.35	1	0.35	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	30	4.7	1.1E-05	9.5E-06	1.1E-05
SILVER	0.25	1	0.25	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	1	4.7	6.5E-05	5.5E-05	6.5E-05
THALLIUM	0.01	1	0.01	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	110		3.2E-08	2.8E-08	3.2E-08
ZINC	0.02	1	0.02	1	NC	NC	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	110		4.8E-06	4.3E-06	4.8E-06
BENZENE	0.08	1	0.08	1	0.08	1	1	1	1	1	1	1	1	1	1	1	1	1	21				
Bis(2-ethylhexyl)PHTHALAT	0.02	1	0.02	1	0.02	1	1	1	1	1	1	1	1	1	1	1	1	1	1				
CARBON TETRACHLORIDE	0.1	1	0.1	1	0.1	1	1	1	1	1	1	1	1	1	1	1	1	1	1				
CHLOROBENZENE	0.1	1	0.1	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	10				
CHLOROFORM	0.1	1	0.1	1	0.1	1	1	1	1	1	1	1	1	1	1	1	1	1	3				
1,1-DICHLOROETHANE	0.13	1.3	0.13	1	NC	NC	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3					
1,2-DICHLOROETHANE	0.1	1	0.1	1	0.1	1	1	1	1	1	1	1	1	1	1	1	1	1					
1,1-DICHLOROETHYLENE	0.1	1	0.1	1	0.102	1	1	1	1	1	1	1	1	1	1	1	1	1					
1,2-DICHLOROETHYLENE	0.1	1	0.1	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1					
ETHYLBENZENE	0.2	1	0.2	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	10				
ETHYLENE DIBROMIDE	0.1	1	0.1	1	0.1	1	1	1	1	1	1	1	1	1	1	1	1	1					
METHYLENE CHLORIDE	0.1	1	0.1	1	0.1	1	1	1	1	1	1	1	1	1	1	1	1	1					
METHYL ETHYL KETONE	0.1	1	0.1	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	600				
METHYL TERT BUTYL ETHER	0.1	1	0.1	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	42				
PHENOL	0.26	1	0.26	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1					
PCB	0.067	0.85	0.067	1	0.85	0.067	1	1	1	1	1	1	1	1	1	1	1	1			9.4E-07	4.3E-06	3.6E-06
TETRACHLOROETHYLENE	0.1	1	0.1	1	0.1	1	1	1	1	1	1	1	1	1	1	1	1	1	11				
TOLUENE	0.12	1	0.12	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	29				
1,1,1-TRICHLOROETHANE	0.1	1	0.1	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	30				
TRICHLOROETHYLENE	0.1	1	0.1	1	0.1	1	1	1	1	1	1	1	1	1	1	1	1	1	5				
VINYL CHLORIDE	0.1	1	0.1	1	1.53	0.16	1	1	1	1	1	1	1	1	1	1	1	1					
XYLENES	0.12	1	0.12	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1	40				
CYANIDE	0.3	1	0.3	1	NC	NC	1	1	1	1	1	1	1	1	1	1	1	1					

TOXICITY INFORMATION

TOXICITY INFORMATION

OIL OR HAZARDOUS MATERIAL

PAHs(LISTED BELOW)

	RAF SC SOIL DERMAL	RAF Ch SOIL INGEST	RAF Ch SOIL DERMAL	RAF SC WATER INGEST	RAF Ch WATER INGEST	RAF Ca WATER INGEST	RAF Ca WATER INGEST	RAF SC VEG INGEST	RAF Ch VEG INGEST	RAF Ca VEG INGEST	SOIL BACKGROUND mg/kg	GV BACKGROUND ug/liter	INDOOR AIR BACKGROUND ug/cu m (VAPORS)	VEG CANCER RISK MULT INGEST 1/day	VEG SUBCH HI MULT 1/day	VEG CHROM HI MULT INHAL 1/day
ACENAPHTHENE	0.2	0.91	0.2	1	0.91	1	NC	1	0.91	1	NC	0.5			3.5E-05	3.0E-05
ACENAPHTHYLENE	0.18	0.91	0.18	0.91	0.91	0.91	NC	0.91	0.91	0.91	NC	0.5			3.5E-05	3.0E-05
ANTHRACENE	0.29	1	0.29	1	1	1	NC	1	1	1	NC	0.5			3.5E-05	3.0E-05
BENZO(a)ANTHRACENE	0.18	0.91	0.18	0.91	0.91	0.91	0.2	1	0.91	0.91	1	0.5		6.9E-06	3.5E-05	3.0E-05
DIBENZO(a,h)ANTHRACENE	0.08	0.91	0.08	0.91	0.91	0.91	0.09	1	0.91	0.91	1	0.5		6.9E-06	3.5E-05	3.0E-05
BENZO(a)PYRENE	0.18	0.91	0.18	0.91	0.91	0.91	0.2	1	0.91	0.91	1	0.5		6.9E-06	3.5E-05	3.0E-05
BENZO(b)FLUORANTHENE	0.18	0.91	0.18	0.91	0.91	0.91	0.2	1	0.91	0.91	1	0.5		6.9E-06	3.5E-05	3.0E-05
BENZO(g,h,i)PERYLENE	0.18	0.91	0.18	0.91	0.91	0.91	NC	1	0.91	0.91	NC	0.5		6.9E-06	3.5E-05	3.0E-05
BENZO(k)FLUORANTHENE	0.18	0.91	0.18	0.91	0.91	0.91	0.2	1	0.91	0.91	1	0.5		6.9E-06	3.5E-05	3.0E-05
CHRYSENE	0.18	0.91	0.18	0.91	0.91	0.91	0.2	1	0.91	0.91	1	0.5		6.9E-06	3.5E-05	3.0E-05
FLUORANTHENE	0.2	1	0.2	1	1	1	NC	1	1	1	NC	0.5			3.5E-05	3.0E-05
FLUORENE	0.2	1	0.2	1	1	1	NC	1	1	1	NC	0.5			3.5E-05	3.0E-05
INDENOC(1,2,3-cd)PYRENE	0.18	0.91	0.18	0.91	0.91	0.91	0.2	1	0.91	0.91	1	0.5		6.9E-06	3.5E-05	3.0E-05
2-METHYLNAPHTHALENE	0.1	1	0.1	1	1	1	NC	1	1	1	NC	0.5			3.5E-05	3.0E-05
NAPHTHALENE	0.1	1	0.1	1	1	1	NC	1	1	1	NC	0.5			3.5E-05	3.0E-05
PHENANTHRENE	0.18	0.91	0.18	0.91	0.91	0.91	NC	0.91	0.91	0.91	NC	0.5			3.5E-05	3.0E-05
PYRENE	0.2	1	0.2	1	1	1	NC	1	1	1	NC	0.5			3.5E-05	3.0E-05

TABLE 7-1 *CONTINUED...*

References for the *ShortForm Toxicity Values*

<u>Reference #</u>	<u>Description</u>
1.	U.S. EPA <i>Integrated Risk Information System</i> (IRIS). On-line search: current as of September 2, 1992.
1.a.	The oral Carcinogenic Potency Value from IRIS is used as a dermal CPV.
1.c.	The chronic inhalation RfC (from IRIS) has been used here as a subchronic inhalation RfC equivalent.
1.d.	This toxicity value for CHROMIUM is taken from the IRIS file for hexavalent chromium (Cr VI).
1.e.	The chronic oral RfD (from IRIS) has been used here as a subchronic oral RfD equivalent.
1.f.	This oral Carcinogenic Potency Value equivalent for arsenic is back-calculated from a drinking water Unit Risk value from IRIS.
1.g.	This Carcinogenic Potency Value or Unit Risk for benzo[a]pyrene (from IRIS) has been applied to the seven PAH compounds which are designated as category A, B1, B2 or C carcinogens.
2.	U.S. EPA <i>Health Effects Assessment Summary Tables</i> (HEAST), Annual FY-1992. [OERR 9200.6-303 (92-1), NTIS No. PB92-921199] March, 1992.
2.a.	The oral Carcinogenic Potency Value from HEAST is used as a dermal CPV.
2.b.	This subchronic oral RfD (from HEAST) for naphthalene has been used as the subchronic oral RfD equivalent for all PAH compounds for which subchronic oral RfDs are unavailable.
2.c.	The chronic inhalation RfC (from HEAST) has been used here as a subchronic inhalation RfC equivalent.
2.d.	The chronic oral RfD for food (from HEAST) has been used as the oral RfD for cadmium.
2.e.	The chronic oral RfD for cadmium (from HEAST) has been used here as a subchronic oral RfD equivalent.
2.f.	The chronic oral RfD for naphthalene (from HEAST) has been used as the chronic RfD equivalent for all PAH compounds for which chronic oral RfDs are unavailable.
2.g.	This toxicity value for CHROMIUM (taken from HEAST) is for hexavalent chromium (Cr VI).
2.h.	This Carcinogenic Potency Value or Unit Risk was taken from a fact sheet distributed by the U.S. EPA Superfund Health Risk Technical Support Center at ECAO-Cincinnati, current as of September 2, 1992.
2.i.	The oral Carcinogenic Potency Value (from the ECAO-Cincinnati fact sheet) is used here as a dermal CPV.

TABLE 7-1 CONTINUED...

References for the ShortForm Toxicity Values

<u>Reference #</u>	<u>Description</u>
3.	Allowable Threshold Concentrations (ATCs) from MA DEQE (1989a), <i>Guidance for Disposal Site Risk Characterization and Related Phase II Activities - In Support of the Massachusetts Contingency Plan</i> , Appendix J.
3.a.	The chronic inhalation ATC (from MA DEQE, 1989a) has been used here as a subchronic inhalation ATC equivalent.
3.b.	The ATC for "total concentration of naphthalene and 2-methylnaphthalene" is used here as the ATC for this chemical.
3.c.	The chronic inhalation ATC for naphthalene has been used as the chronic inhalation RfC equivalent for all PAH compounds for which chronic inhalation RfCs are unavailable.
3.d.	The chronic inhalation ATC for naphthalene has been used as the subchronic inhalation RfC equivalent for all PAH compounds for which subchronic RfCs are unavailable.
4.	Developed for the <i>Residential ShortForm</i> by MA DEP staff. Documentation of this value may be found in APPENDIX D.
NC	Not Calculated

8.0 EXPOSURE ASSESSMENT

8.1 Introduction

Exposure assessment is the link between hazard identification, dose-response assessment and risk characterization. An exposure assessment concerns itself with identification of receptors, exposure pathways, exposure points, exposure routes, and frequency, duration and magnitude of exposures.

8.2 Basic Approach/Assumptions

The basic approach used in this exposure assessment is that the most useful assessment is one which is realistic and health protective. This assessment is not a worst case exposure assessment. Worst case assessments are useful screening tools which may demonstrate that risks are clearly insignificant, but they are not useful in determining whether realistic risks are actually significant (US EPA, 1988).

This assessment consciously uses some intake rates, contact rates and bodyweights which represent mid-range estimates of the possible values for each of those parameters. Arithmetic means of concentrations at exposure points are recommended for use in the risk calculations. "Upper bound" (conservative, health protective) estimates of cancer potency factors are used in the assessment. The Reference Doses, Inhalation Reference Concentrations and Threshold Effects Exposure Limits used in the assessment are all considered health protective and very conservative. The values used for frequency and duration of exposure are intended to reflect realistic values for Massachusetts and the climatic conditions in Massachusetts. This mix of mid-range, realistic exposure assumptions and "upper bound" or conservative, health protective toxicity values is intended to produce realistic risk estimates. These estimates are considered to be protective of public health in that they are not likely to be underestimates of the "true risk". (See Section 10 - Uncertainty Analysis.)

8.3 Receptors

8.3.1 Maximally Exposed Individual

This residential scenario concerns itself with theoretical on-site residents and the exposures they might experience.

The exposure parameters and assumptions are targeted to average exposures for the maximally exposed individual in this receptor group. In this context, the maximally exposed individual is that person whose activities realistically result in the exposure via all of the realistic exposure pathways at that location. For example, at a residence with soil and drinking water contamination, with vapor problems associated with groundwater or subsurface soil contamination, and a garden, the individual who plays or works in the yard regularly, drinks and showers with tap water, eats homegrown fruits and vegetables, and breathes vapors in the home would be the maximally exposed individual.

A Visitor/Trespasser Receptor is not explicitly evaluated in this assessment although there is certainly opportunity for visitors or trespassers to be exposed at a "residential" disposal site. Once a decision has been made that a location has a current or foreseeable use which is "residential," then the visitor/trespasser would have lower frequency and daily duration of soil exposures and indoor vapor inhalation than the resident. The visitor would also experience lower (if any) drinking water and fruits/vegetable intakes. The visitor/trespasser would only be important if "residential" use did not become a reality and an on-site receptor is irrelevant. In such a case, however, the use of the *Residential ShortForm* might not be appropriate (it would overestimate risks).

The exposure assessment must characterize exposures in a way which is compatible with the risk characterization approach. In this assessment, the risk characterization is conducted via Method 3b of the Massachusetts Contingency Plan (310 CMR 40.545(3)(g)3.b.). Method 3b requires the comparison of exposure point concentrations to promulgated public health standards and it requires that Total Sites Risks be characterized for both cancer risk (expressed as excess lifetime cancer risk [ELCR]) and non-cancer risk (expressed as a Hazard Index [HI]). The risk characterization requirements of the MCP are discussed in more detail in Section 9.0.

In this Residential Scenario, exposure point concentrations are directly employed to characterize exposures for the purpose of (1) comparison to drinking water standards and (2) for the calculation of HI and ELCR for volatile organic compound inhalation exposures indoors. Average daily contaminant doses are employed to characterize exposures for the

purpose of calculating HI and ELCR for soil ingestion, soil dermal contact, fruits and vegetable, and drinking water exposures.

Although exposure is often defined as the amount of contaminant available at an exchange boundary (lung, gastrointestinal tract), a broader definition of exposure assessment is used here. The estimation of both exposure rates and dose rates are included in this exposure assessment.

8.3.2 Age Groups

While the *Residential ShortForm* assessment is performed for the maximally exposed receptor, identified as the resident who lives on or near the disposal site for up to 30 years, risk estimates are generated for different age periods in that receptor's lifetime. This methodology has been adopted in the knowledge that exposure is not constant over a receptor's lifetime, but in fact varies with age-related factors such as body weight and patterns of activity. The variation in exposure rate over the course of the receptor's lifetime is particularly relevant for the evaluation of threshold health effects: it is important to identify the age group(s) which represent the highest subchronic and chronic exposure periods. A risk analysis which focuses on these identified age groups will be adequately protective of all stages of the receptor's life and will substantially reduce the number of risk characterizations necessary to assess the disposal site. It is unnecessary, for example, to calculate an Excess Lifetime Cancer Risk for a childhood exposure if the calculation is also performed for the receptor's duration of residence (30 years) and that period includes childhood.

The age groups which are the focus of this exposure assessment are:

- ages 1-2 years: for subchronic exposures and threshold effects;
- ages 1-8 years: for chronic exposures and threshold effects; and
- ages 0-30 years: for carcinogenic effects.

The selection of age groups for subchronic and chronic exposure evaluation is based on the following definitions of the terms *subchronic* and *chronic* with respect to human exposures: subchronic is an exposure greater than 30 days but less than 7 years; chronic is an exposure of 7 years or more. The age groups are selected as follows.

For *subchronic exposures*, the age group evaluated has the highest total exposure (all pathways) for any period greater than 30 days but less than 7 years.

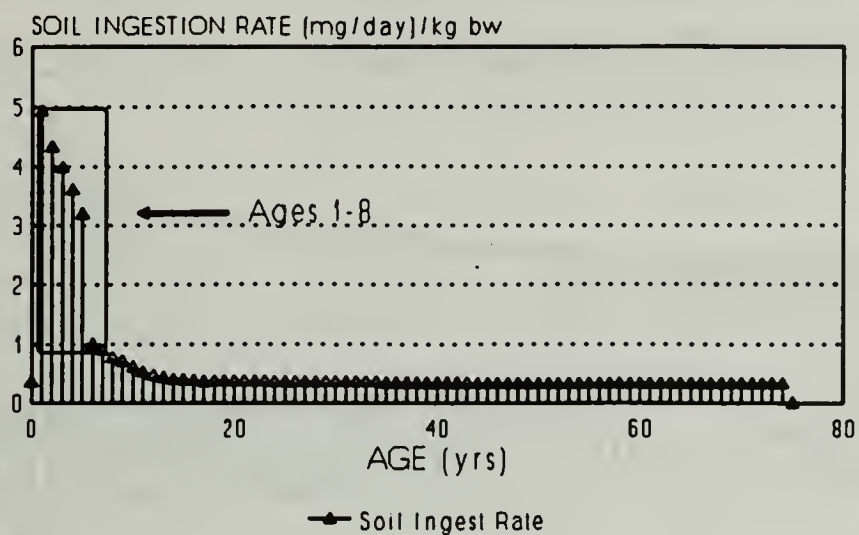
For *chronic exposures*, the age group evaluated has the highest total exposure (all pathways) for any period equal to or greater than 7 years.

Visual inspection of the graphs in Figures 8-1 through 8-3 indicates that exposure to soil, drinking water, and fruits and vegetables is highest during the childhood years, falls off, and then remains fairly constant as age increases. The exposure to indoor air (Figure 8-4) appears marginally higher in the childhood years than in other portions of the lifetime.

It is clear that the age 1-2 years is associated with the highest exposure for any period less than seven years in duration and is therefore the age group which is appropriate for subchronic exposure characterization. In a like manner it appears that children aged 1-8 years experience the highest exposure rate (all pathways) of any age group representing an exposure period of 7 or more years duration. Therefore, the age group 1-8 years was chosen the appropriate exposure period for the assessment of risks for chronic threshold effects.

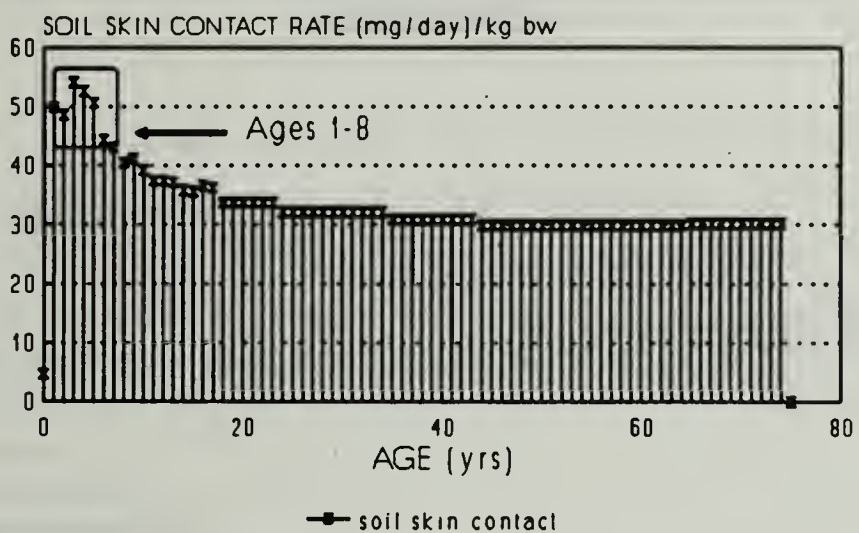
NOTE: The graphs in Figures 8-1 through 8-4 depict medium specific exposure rates (not contaminant exposure rates). The exposure rates for direct soil contact, drinking water exposures, fruit and vegetable ingestion and inhalation of indoor air incorporate the intake and contact rates as well as the frequencies and durations used in this assessment. These graphs do not incorporate contaminant concentrations nor Relative Absorption Factors (RAF). Of course, the contaminant concentrations may vary greatly from site-to-site and from chemical-to-chemical at a given site. The RAFs also vary by chemical and medium. The combination of contaminant concentration and RAF in conjunction with the medium-specific exposure rates produce the contaminant specific exposure rates. The contaminant exposure rates are therefore *not* generalizable and the medium-specific exposure rates are used here *only* to select age groups for subchronic and chronic exposures used in threshold effects risk assessment.

SOIL INGESTION RATE vs AGE RATE NORMALIZED TO BODYWEIGHT



DEP 1991 a

SOIL DERMAL CONTACT RATE vs AGE RATE NORMALIZED TO BODYWEIGHT



DEP 1991 a

FIGURE 8-1

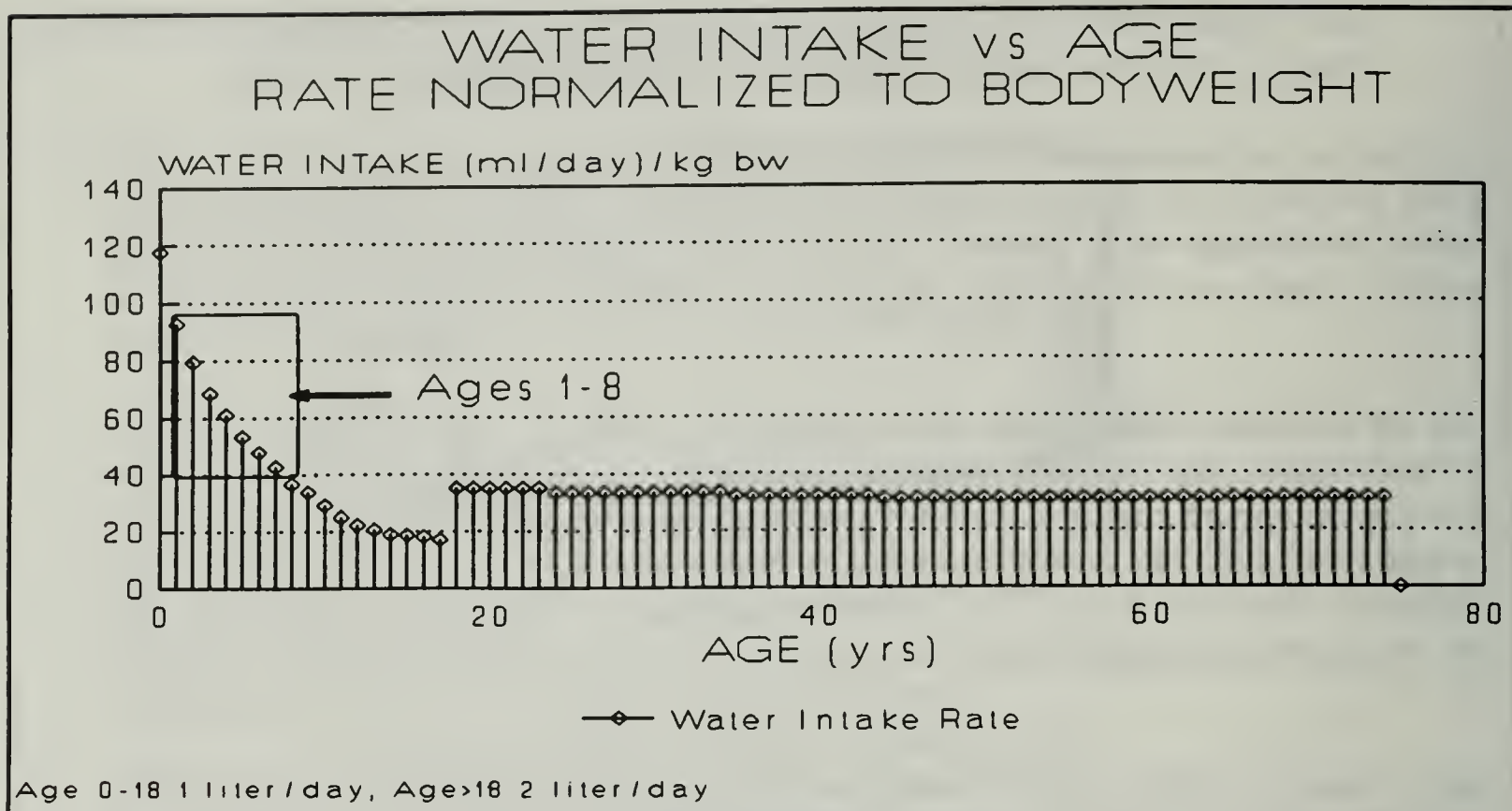


FIGURE 8-2

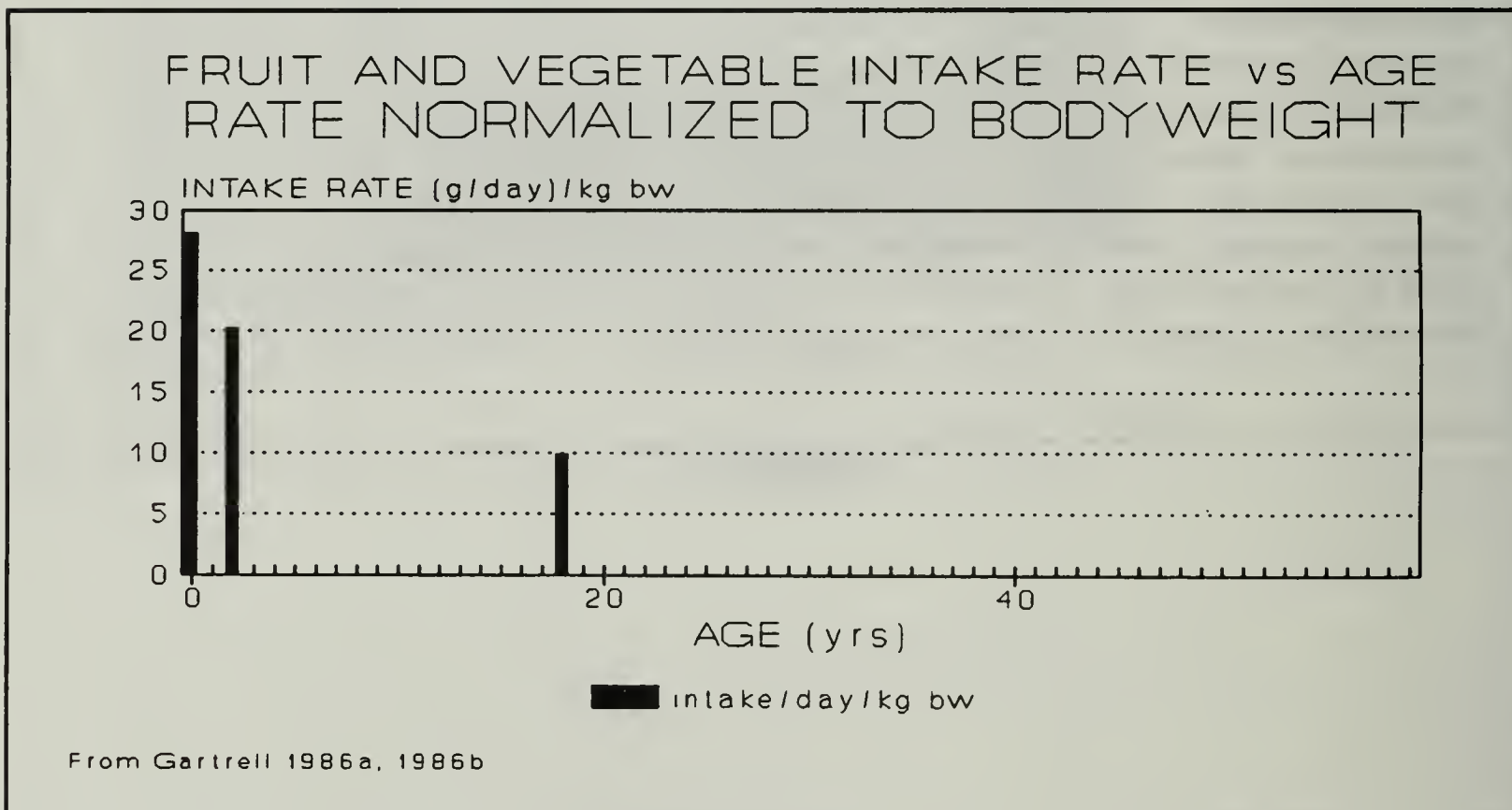


FIGURE 8-3

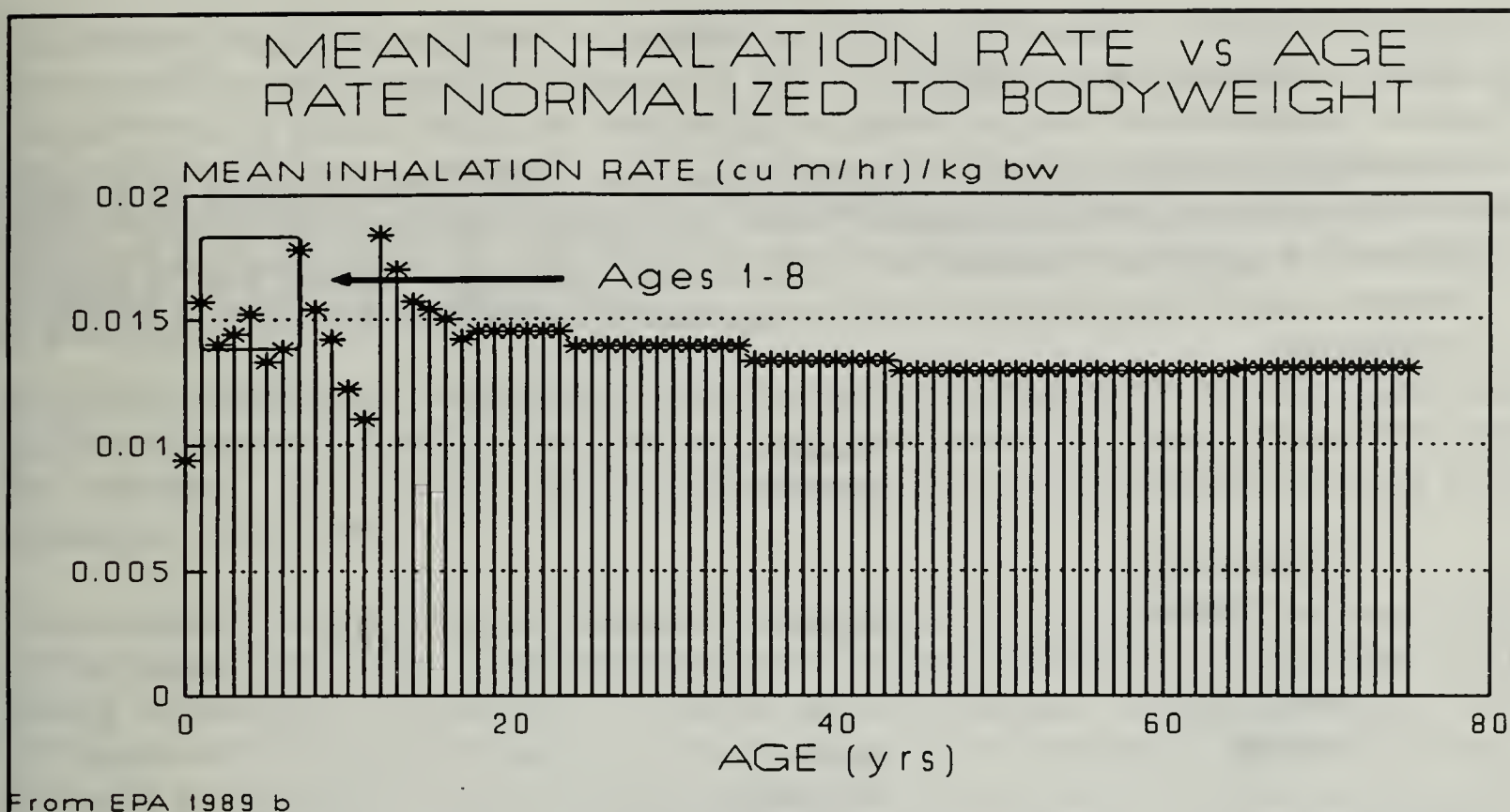


FIGURE 8-4

8.4 Potential Exposure Pathways

The following list of exposure pathways comprises the universe of pathways which are potentially important and may require quantitative evaluation for a "residential" scenario.

- Soil ingestion
- Soil dermal contact
- Fugitive dust inhalation
- Fruits and vegetables ingestion
- Drinking water ingestion
- Drinking water dermal contact
- Indoor Vapor inhalation related to showering
- Indoor Vapor inhalation related to other domestic water use
- Indoor Vapor inhalation related to subsurface soil or groundwater

NOTE: No surface water-related exposures are considered. If contaminated surface water represents a potential exposure medium at a particular residential site, then a supplemental human health risk assessment may be required, with the results then combined with those produced by the *Residential ShortForm*. Alternatively, all the exposure pathways related to the site could be evaluated without the aid of the *ShortForm*.

8.5 Pathways Evaluated

An evaluation of these potential exposure pathways resulted in the following list of pathways which are evaluated quantitatively. Note that version 1.6a of the *Residential ShortForm* allows the quantitative evaluation of all of these pathways. Version 1.6b is identical to version 1.6a with the exception that the ingestion of homegrown fruits and vegetables is not considered.

Soil:	ingestion dermal contact
Fruits and Vegetables:	ingestion (v. 1.6a only)
Drinking water:	ingestion dermal contact
Indoor vapor: (from showering)	inhalation
Indoor vapor: (from subsurface soil or groundwater)	inhalation

Inhalation of fugitive dust is not quantitatively evaluated in this assessment because the magnitude of that exposure is insignificant for a residential scenario where soil ingestion and soil dermal contact exposures are also occurring. The technical documentation which supports this conclusion is found in Section 8.8.

Indoor vapor inhalation related to non-showering domestic use of tap water was not explicitly evaluated here. However, the indoor vapor pathway (primarily related to subsurface soil or groundwater) may account for the vapors generated by non-showering domestic tap water use. It is *strongly* recommended that the indoor vapor pathway is evaluated using only in-home vapor concentration measurements (not modelled concentrations). Measurement of vapors indoors would quantify vapors in the home from any number of sources including fuel storage, migration into the residence from subsurface soil and groundwater, release of volatiles from domestic water use, and domestic use of solvent - containing products.

The shower-related vapor inhalation exposure is evaluated separately in order to include the short-duration, high intensity exposure in the shower which would not be adequately characterized by typical indoor air monitoring programs designed to characterize "average" subchronic or chronic exposures. In this assessment, the measured indoor vapor concentrations used to evaluate non-showering related vapor problems are not based on any bathroom air quality samples. The shower related vapor inhalation pathway evaluated here is limited to bathroom exposures only.

No surface water-related exposures were considered here. Recreational dermal contact and incidental ingestion of surface water and sediment and ingestion of locally caught fish were not evaluated. At some later date, these pathways may be incorporated into the *Risk Assessment ShortForm*.

Some exposure pathways are not evaluated via the use of measured concentrations of OHM in the exposure medium. These pathways are (1) dermal absorption of OHM from water during showering, (2) inhalation of OHM vapors generated during showering and (3) ingestion of OHM from fruits/vegetables grown in contaminated soil. Exposures for these pathways are quantified by using models to generalize the magnitude of these exposures in comparison to drinking water ingestion or by modeling exposure point concentrations. Dermal absorption exposures of OHM during showering are assumed to be roughly equivalent to ingestion exposures for volatiles and semi-volatiles, as described in Section 8.9. [** This pathway is under review, and future versions of the *Residential ShortForm* may adopt an alternative model.] Inhalation exposure to volatiles generated during showering is assumed to be roughly equivalent to drinking water ingestion exposures, as described in Section 8.9. [** This pathway is also under review, and future versions of the *Residential ShortForm* may adopt an alternative model.] The model used to estimate exposures to OHM from ingestion of fruits and vegetables is provided in Section 8.10. [** The homegrown fruits and vegetables pathway is currently under review, and future versions of the *Residential ShortForm* may adopt an alternative model.]

Optionally, when it is impossible or infeasible to measure exposure point concentrations (when the exposure is not yet occurring or OHM has not yet reached the exposure point), modeled exposure point concentrations are appropriate for all drinking water exposures, including ingestion.

8.6 Exposure Point Concentrations

This section identifies the approach and techniques used to identify exposure point concentrations for use in the risk assessment.

8.6.1 Identification Of Exposure Points

Exposure points describe an area of a disposal site or surrounding environment, not necessarily a single, discrete point. It is at the Exposure Point that the receptor is assumed to be exposed to the oil or hazardous material, resulting in some increase in risk of harm to the receptor's health.

It is not unlikely that a receptor is exposed to contamination related to a given disposal site at multiple exposure points. For example, the resident receptor who is the subject of the *Residential ShortForm* may be exposed to contaminants in drinking water in the home while being exposed via direct contact with contaminated soil at a local playground. In more complicated scenarios, the risk assessor may identify multiple Exposure Points for the same route of exposure (direct contact with soil).

Before the *Residential ShortForm* is employed the risk assessor must clearly identify all the potential Exposure Points to be evaluated.

8.6.2 Identification/Estimation Of Exposure Point Concentrations

This section addresses the issues involved in identifying and estimating exposure point concentrations. Guidance is given on how to estimate exposure point concentrations that are representative of disposal site conditions. The selection of analytical data that are representative of exposures and the manner in which these data, including non-detects and trace values, are incorporated into the calculation of average exposure point concentrations are discussed.

Though direct measurement of exposure point concentrations is preferred, estimation of exposure point concentrations may be acceptable. Measured concentrations may serve as input to models which predict emissions, fate, transport or persistence. Modeling methods should be fully referenced and described. Some general guidelines and references for estimating exposure point concentrations are presented.

8.6.2.1 Selection of Analytical Data for Estimation of Exposure Point Concentrations

Analytical data will be generated during the MCP Phase II Comprehensive Site Investigation in order to characterize the nature, concentration, and horizontal and vertical distribution of the oil and hazardous materials at the disposal site. This data collection phase also provides analytical data for use in the Phase II risk assessment, and care must be given to insure that the resulting data meet the requirements of the risk assessor. A sampling plan should be developed in consultation with the risk assessor.

Analytical data for samples which are representative of actual or potential exposures should be selected for use in estimating representative exposure point concentrations.

- If exposures are confined to a particular portion of the site only data taken from these areas should be included in the estimation of representative exposure point concentrations.
- If exposures predominate in one area, data from these areas should be weighted and incorporated into the calculation of exposure point concentrations accordingly.
- In addition, samples taken in inaccessible locations should not be considered when evaluating exposures via ingestion or dermal contact with surface soils. For example, use of data from samples taken under buildings or at a depth of ten feet may be appropriate only when there is a foreseeable mechanism for bringing humans into contact with the soil contaminants (e.g. excavation during construction, or a seasonal high water table which brings subsurface contaminants to the surface).

8.6.2.2 Treatment of Non-Detects in the Estimation of Exposure Point Concentrations

In estimating exposure point concentrations, it is not uncommon for the risk assessor to be presented with analytic data for a chemical at the site which includes a number of samples reported to be below the Method Detection Limit (MDL). Such results are referred to as "*Non-Detects*".

Non-Detect results may be classified into two general situations. *First*, if a chemical is truly not present at the disposal site (virtually all the samples are reported as Non-Detect), and there is no history of a release of that chemical, *then the risk assessor may conclude that the chemical be dropped from the quantitative risk assessment.* *Second*, if the chemical is reported at the site at concentrations ranging from Non-Detect to some site maximum, then the risk assessor may conclude that the reported Non-Detects actually represent a distribution of concentrations between zero and the MDL. These Non-Detect results contribute to the information known about the disposal site and should be incorporated into the quantitative risk assessment in a meaningful way. [There is a third possible situation, where the spatial pattern of

positive and Non-Detect results indicate that contamination is localized to specific areas. This would represent a combination of the previous two examples.]

There are several options for the treatment of "non-detects" described in the literature (Travis, 1990; Helsel, 1990; Haas, 1990 Klassen, 1986). The methodologies described include the use of log-probit analysis, maximum likelihood estimation and probability plotting procedures. The level of effort and number of data points required to effectively employ these methods vary, and the risk assessor is encouraged to exercise professional judgement in the selection of a method to treat the Non-Detect results.

It is the Department's recommendation, however, that for the majority of Chapter 21E disposal sites a more straightforward approach is often appropriate:

When a contaminant is known to be present in the area under investigation and the laboratory reports the concentration of an OHM in a sample taken from the area as "Non-Detect", the concentration of the OHM in that sample should be assumed to be one-half of the Practical Quantitation Limit (PQL) (or the Method Detection Limit, MDL).

This methodology (using 1/2 the MDL) for Non-Detect values suffers from the twin sins of being easy to understand and facile to implement. These benefits must be weighed against the bias which is introduced in the resulting EPC estimate. The ND method selection should also consider, however, the often high level of uncertainty which is inherent in environmental sampling and analysis procedures, resulting from a failure to take an adequate number of samples, from mistakes on the part of the sampler, from the heterogeneity of the matrix being sampled, and from intentional bias in the sample collection. For relatively small disposal sites, these inherent uncertainties may overwhelm the bias introduced by using 1/2 the MDL. A more statistically oriented ND method may not, in such cases, significantly reduce the uncertainty inherent in the resulting EPC. It is up to the risk assessor to judge the level of sophistication appropriate to the data set.

As always, there may be exceptions to this guidance, particularly when detection limits are unusually high, or when the site history and the NDs may indicate the *absence* of an OHM at a site (or areas within site). In the latter case, the chemical may be dropped from the quantitative risk assessment or the NDs may be factored into the Exposure Point Concentration as a zero value with appropriate justification.

8.6.2.3 Calculating Exposure Point Concentrations

The exposure point concentrations should be calculated in a way that is consistent with its ultimate use or the standard to which it will be compared.

In comparing EPCs to applicable or suitably analogous standards, attention should be given to whether the standards represent averages over time (e.g., the arithmetic mean of four quarterly samples for the Massachusetts Maximum Contaminant Levels). Generally the text of the regulations containing the standards will describe how to develop concentrations which are comparable to the standards. Such guidance usually includes sampling methodology as well as any averaging procedures.

For the purposes of quantitative risk assessment, the frequency and distribution of both sampling data and exposures should be considered: sampling data should be appropriately weighted to represent actual exposures. Guidance is provided below for a variety of situations likely to be encountered.

As exposure to contaminants at a disposal site is a function of both time and space, the most appropriate measure of concentration to use to derive an EPC is the arithmetic mean.

Because sampling data and exposures are not necessarily distributed uniformly across the site, consideration should be given to actual or potential exposure patterns as well as the sampling frequency across the site. At any given site, the following scenarios are possible:

- Frequency of sampling data may be unequally distributed across the site;
- Frequency of exposure may be unequally distributed across the site;
- Both frequency of sampling data and frequency of exposures may be unequally distributed across the site (these distributions may or may not be coincident);
- Both frequency of sampling data and frequency of exposures may be equally distributed across the site (these distributions may or may not be coincident).

The calculation of representative exposure point concentrations should take these exposure patterns and sampling frequencies into account. At least two methods may be used to account for unequal exposures or unequal sampling frequency. The first method involves estimating a weighted average exposure point concentration. A weighted average exposure point concentration is considered a representative estimation of exposures at a given site. In this method, analytical data should be weighted in a manner which reflects the exposure patterns and the sampling frequency in the areas of actual or potential exposures.

EXAMPLE: If 20 equidistant samples were taken in a portion of a site approximately 50 meters by 50 meters, each sample can be said to represent 125 m^2 ($2500 \text{ m}^2 / 20 \text{ samples}$). If three additional equidistant samples were obtained from another portion of the site approximately 100 meters by 100 meters (in order to verify the assumption that the area was free of contamination) each sample could be said to represent 3333 m^2 . If exposures are equally likely throughout the entire site, the sample values should be weighted according to the relative area each represents. If exposures are not equally likely throughout the site, sample values should be weighted according to both the relative area each sample value represents as well as the relative exposure likelihood in each area. Only data which represent actual or potential areas of exposure should be incorporated. The weighted average exposure point concentrations obtained from this exercise would be used as inputs to any emission models, transport models, or persistence models which require an average concentration for OHM present at the site.

The second method involves calculating separate risks using the *Residential ShortForm* for each subarea of exposure and then weighting the resulting risks to estimate a Total Site Risk which reflects exposure patterns at the entire site.

EXAMPLE: At a given site, 90 percent of the exposure time takes place on half of the site and 10 percent of the exposure time takes place on the other half of the site. The average exposure point concentration for the first half of the site should be calculated (sample frequency should be considered when calculating this average value). The average exposure point concentration for the remaining half of the site, upon which only 10 percent of total exposure time takes place, should also be calculated. Total Site Risks dose for the entire site would weigh the separate Total Risks from each area according to the relative time of exposure in each area.

8.6.2.4 Evaluation of Acute Exposures.

The *Residential ShortForm* does not evaluate potential risks associated with acute (up to one month) exposures. It is left to the risk assessor to independently evaluate such exposures at any time during the site assessment process to identify potential Imminent Hazards. In cases when short term exposures may result in adverse health effects, it would be important to consider the highest concentrations to which an individual may be exposed during this short period of time. In the case of acute exposure evaluations, a maximum reported value, or the arithmetic mean of data points in a small area would be chosen to represent the exposure point concentration.

8.6.2.5 Modeling of Exposure Point Concentrations

Though direct measurement of contaminants is preferred for use in the *Residential ShortForm*, there are times when it is necessary to estimate exposure point concentrations through the use of mathematical models. Exposures may be expected via air, groundwater, or soil, though analytical data may not be available for each relevant medium. Mathematical models can be used to estimate emissions, fate and transport, or persistence of contaminants in the environment and to estimate the concentrations of OHM at exposure points when measured data are not available.

Mathematical models refer to analytical solutions that can be performed using a hand calculator, or analytical or numerical models implemented as programs to be run on a computer.

In the absence of measured data, the need for mathematical modeling should be based on an assessment of the potential mobility of the contaminant from the location in which it was originally discovered to locations where exposure is likely to occur. For example, if contamination was originally discovered in soil, important questions to consider include the following:

- Is leaching of OHM possible?
- Is release to groundwater possible?
- Is volatilization release to air possible?

Models that predict either intramedia or intermedia transport should consider site-specific as well as chemical-specific parameters. Potentially relevant site specific parameters include meteorological data, soil type, bulk density and porosity, stream velocity, and hydraulic conductivity. Potentially relevant chemical specific parameters include the appropriate phase transfer coefficients, Henry's Law Constant, vapor pressure and solubility.

Models must also be able to simulate the relevant physical processes occurring within the specified environmental setting. These processes may include adsorption, attenuation, diffusion, dispersion, volatilization, erosion or density effects related to temperature and concentration.

The data selected as inputs to mathematical models should be selected carefully and should be representative of the actual area where emissions contributing to exposures are occurring. If an average contaminant concentration is required as input to the model, the concentration would generally be the weighted arithmetic mean of all data for the medium of concern in the appropriate area during a sampling event.

Techniques for modeling emissions, persistence and transport of OHM should be generally accepted and well documented. If models are commercially available, complete references including a brief discussion of the models input coefficients, assumptions and uncertainties should be provided. If models are not commercially available, source codes or other documentation which allows technical review of the model and a more complete discussion of the models input coefficients, assumptions and uncertainties should be provided.

8.7 Soil - Direct Contact

The soil exposure assessment described in this section is extracted from an ongoing project within the Department to develop methodology for deriving soil advisory levels (MA DEP, 1991a).

8.7.1 Narrative Description

Incidental ingestion of and dermal contact with surface soils and dust have been identified as potential exposures of concern for both children and adults in residential settings.

In the scenario developed for the *Residential ShortForm*, the receptor's exposure to contaminated soil and dust varies seasonally. Outdoor exposures are limited to 5 days per week during the months of May through September (a period of 153 days). During this time, it is assumed that the literature values for soil ingestion rates (LaGoy, 1987) represent the sum of the outdoor soil exposures and indoor dust exposures on days when exposure occurs. During the colder months (212 days), the receptor is assumed to be exposed "indoors only" and the exposures are assumed to occur primarily by hand contact with dust with subsequent mouthing behavior. This "indoor only" exposure has been applied to children 1-6 years of age.

The exposure rate normalized to bodyweight is most often the expression of exposure which is of most toxicological significance. This concept is particularly important in the assessment of direct soil contact because the soil exposure rate normalized to bodyweight is not constant over the lifetime (as demonstrated in Figure 8-1), but rather is relatively high in young children and falls off to a lower, fairly constant level in adults. Knowledge about the age dependent variability of the soil exposure rate can be used to choose the appropriate age groups to consider for subchronic and chronic exposures, and which 30-year period of the receptor's life to select for the evaluation of cancer risk, as described in Section 8.3.2.

In this assessment, chemical exposures are a function of the concentration of an OHM in soil and the average soil exposure rate normalized to bodyweight for various exposure durations and age groups. The concentrations of OHM are assumed to remain constant in soil over time, although a more sophisticated analysis could conceivably include a decay function. As described below, the soil ingestion rates and soil dermal contact rates used here incorporate the frequency and duration of exposure and the appropriate averaging period.

8.7.2 Equations

The equation used to evaluate potential non-carcinogenic effects associated with direct contact with contaminated surface soil is given as:

$$HI = \frac{[OHM]_{\text{soil}} * ((NADSIR * RAF) + (NADSCR * RAF)) * C}{RfD} \quad (1)$$

The equation used to evaluate potential carcinogenic effects associated with direct contact exposure with contaminated surface soil is given as:

$$ELCR = [OHM]_{\text{soil}} * ((NLADSIR * RAF) + (NLADSCR * RAF)) * C * CPF \quad (2)$$

where the exposure related terms (not shaded above) are:

[OHM] _{soil} =	The operational Exposure Point Concentrations (EPC) of the <u>oil</u> or <u>hazardous material</u> in surface <u>soil</u> . In units: mg/kg.
NADSIR =	The <u>Normalized Average Daily Soil Ingestion Rate</u> (normalized to bodyweight) for the exposure period of concern. (Table 8-1) These values are rates of <u>soil</u> ingestion (not rates of OHM ingestion). In units: mg _{soil} /kg/day.
NADSCR =	The <u>Normalized Average Daily Soil Dermal Contact Rate</u> (normalized to bodyweight) for the exposure period of concern. (Table 8-1) These values are rates of <u>soil</u> contact (not contact with OHM). In units: mg _{soil} /kg/day.
RAF =	The <u>Relative Absorption Factors</u> for soil ingestion or dermal contact and threshold or cancer health effects (a chemical-, medium-, route-, and health endpoint-specific value). See Appendix C. Dimensionless.
C =	Units <u>Conversion Factor</u> : 1 kg/10 ⁶ mg
NLADSIR =	Time-weighted <u>Normalized Lifetime Average Daily Soil Ingestion Rate</u> (normalized to bodyweight). (Table 8-1) This value represents a 30 year exposure averaged over a lifetime, <u>not</u> a lifetime exposure. In units: mg _{soil} /kg/day.
NLADSCR =	Time-weighted <u>Normalized Lifetime Average Daily Soil Dermal Contact Rate</u> (normalized to bodyweight). (Table 8-1) This value represents a 30 year exposure averaged over a lifetime, <u>not</u> a lifetime exposure. In units: mg _{soil} /kg/day.

The Normalized Average Daily Soil Ingestion Rate, (NADSIR) and the Normalized Average Daily Soil Contact Rate (NADSCR) for subchronic and chronic exposures were used to calculate the subchronic and chronic direct contact Hazard Indices respectively. The Normalized Lifetime Average Daily Soil Ingestion Rates (NLADSIR) and the Normalized Lifetime Average Daily Soil Contact Rates (NLADSCR) are used to calculate the direct contact Excess Lifetime Cancer Risks. The numerical value for each of these soil exposure rates is shown in Table 8-1.

Tables 8-2 through 8-10 document in a step-by-step approach the derivation of the soil ingestion rates and the soil dermal contact rates summarized in Table 8-1. The average exposure rates can be reproduced from the information in these tables and the references cited. All of these exposure rates are based on a methodology described in the DRAFT Development of Soil Advisory Levels, Technical Support Document (MA DEP, 1991a).

TABLE 8-1

SUMMARY OF SOIL INGESTION AND DERMAL CONTACT RATES			
THRESHOLD EFFECTS			
Exposure Type	Age years	Normalized (to BW) Average Daily Soil Ingestion Rate (NADSIR)	Normalized (to BW) Average Daily Soil/Skin Contact Rate (NADSCR)
		mg_{soil}/kg/day	mg_{soil}/kg/day
Subchronic	1-2	4.5	30.6
Chronic	1-8	3.1	28.5
NON-THRESHOLD (CARCINOGENIC) EFFECTS			
	Age years	Normalized (to BW) Lifetime Average Daily Soil Ingestion Rate (NLADSIR)	Normalized (to BW) Lifetime Average Daily Soil/Skin Contact Rate (NLADSCR)
		mg_{soil}/kg/day	mg_{soil}/kg/day
	0 - 30	0.41	7.3
The derivation of these values is presented in the following tables.			

8.7.3 Soil Ingestion Intakes

This section will describe the development of the soil *ingestion* rates used in the *ShortForm* formulae. These values are age specific and are normalized to body weight. The exposure model used to quantify the soil ingestion pathway assumes that some soil intake will occur in the home during winter months, but that the majority of the exposure will be received from indoor and outdoor exposures during the warmer time of the year. As a result of the detailed analysis, each age group experiences a slightly different exposure, and annual average daily soil ingestion rates calculated ranges between 20 to 60 mg of soil per day. The step-wise process followed in the calculation of the exposure rates is summarized below.

STEP 1: Ingestion of indoor dust was considered for young children, aged 1 to 6 years. It is assumed that each exposure event consists of the ingestion of the dust/soil covering the surface of one half of one finger. Table 8-2 develops soil ingestion rates for these indoor exposures, and this information is used in Step 2.

TABLE 8-2

INDOOR-ONLY SOIL INGESTION EXPOSURE

AGE	Skin Surface Area: 1/2 of One Finger ¹	Dust Adherence ²	Fraction of Dust from Soil ³	Frequency of Finger Mouthing Events ⁴	Hours of Exposure per day	Soil Ingested - INDOOR ONLY ⁵
years	cm ² /event	mg/cm ²		events/hour	hrs/day	mg soil/day
						2
1 < 2	7.3	0.056	0.8	9	3	8.8
2 < 3	7.7	0.056	0.8	9	7	21.7
3 < 4	9.9	0.056	0.8	9	7	27.9
4 < 5	10.1	0.056	0.8	9	7	28.5
5 < 6	11.1	0.056	0.8	9	7	31.3
1 -	The surface area of 1/2 of one finger is assumed to be approximately equal to 1/40 the surface area of both hands. The source of the Surface area information is described in more detail in Table 8-6. This value is derived from that table: (Column 2 * Column 3 /100/40).					
2 -	Hawley, 1985; average dust covering indoor surfaces assumed to be the average dust covering finger.					
3 -	Hawley, 1985					
4 -	MA DEQE, 1985					
5 -	The mass of soil ingested as a result of finger mouthing activities. Example, age 1 < 2: $7.3 * 0.056 * 0.8 * 9 * 3 = 8.8 \text{ mg soil/day}$					

STEP 2: An annual average daily soil intake was developed for each age group, as shown in Table 8-3. This value is weighted to reflect the relative time spent outdoors where greater exposure to soil would be expected. The resulting soil ingestion rates are then used in Step 3.

TABLE 8-3

CALCULATION OF AGE-SPECIFIC SOIL INGESTION RATES					
AGE years	SOIL INGESTION RATES ** On days Exposed **		FREQUENCY OF EXPOSURE		ANNUAL AVERAGE 365 days
	Indoor Exposure Only ¹ mg soil/d	Indoor & Outdoor Exposure ² mg soil/d	Indoors Only ³ Oct. -> April of 212 days days	Indoors + Outdoors ⁴ May -> Sept. of 153 days days	DAILY SOIL INGESTION RATE⁵ mg soil/d
< 1	0	0	0	0	0
1 < 2	8.8	100	212	44 + 109 = 153	47.0
2 < 3	21.7	100	212	44 + 109 = 153	54.5
3 < 4	27.9	100	212	44 + 109 = 153	58.1
4 < 5	28.5	100	212	44 + 109 = 153	58.5
5 < 6	31.3	100	212	44 + 109 = 153	60.1
6 < 7	0	50	0	44 + 109 = 153	21.0
7 < 8	0	50	0	44 + 109 = 153	21.0
8 < 9	0	50	0	44 + 109 = 153	21.0
9 < 10	0	50	0	44 + 109 = 153	21.0
10 < 11	0	50	0	44 + 109 = 153	21.0
11 < 12	0	50	0	44 + 109 = 153	21.0
12 < 13	0	50	0	44 + 109 = 153	21.0
13 < 14	0	50	0	44 + 109 = 153	21.0
14 < 15	0	50	0	44 + 109 = 153	21.0
15 < 16	0	50	0	44 + 109 = 153	21.0
16 < 17	0	50	0	44 + 109 = 153	21.0
17 < 18	0	50	0	44 + 109 = 153	21.0
18 < 25	0	50	0	44 + 109 = 153	21.0
25 < 30	0	50	0	44 + 109 = 153	21.0
<p>1 - Indoor ONLY Exposures taken from Table 8-2.</p> <p>2 - Soil Ingestion Rate on days when BOTH Indoor & Outdoor exposures may occur taken from LaGoy (1987)</p> <p>3 - 212 days is approximately 7 days/week from October through April. No outdoor exposure is assumed to occur during this period.</p> <p>4 - 153 days approximates indoor exposures 2 days/week and outdoor exposures 5 days/week during this period.</p> <p>5 - The average daily soil ingestion rate for this age group, adjusted for the frequency of exposure. Example, age 1 < 2 years: $[(8.8 \text{ mg/d} * 212 \text{ d}) + (100 \text{ mg/d} * 153 \text{ d})]/365 \text{ days} = 47.0 \text{ mg soil/day}$ </p>					

STEP 3: The soil ingestion rates from Step 2 are normalized to the body weight of each age group and weighted for the number of years in that age group (This is important for ages 18<25 and 25<30). This calculation is presented in Table 8-4.

TABLE 8-4

CALCULATION OF TIME-WEIGHTED AVERAGE DAILY SOIL INGESTION EXPOSURES NORMALIZED TO BODYWEIGHT				
AGE years	MEDIAN BODY WEIGHT¹ kilograms	SOIL INGESTION RATE² mg soil/day	WEIGHTING FACTOR³ years	DAILY SOIL INGESTION RATE FOR THE TIME PERIOD⁴ (mg * yrs)/(kg * d)
< 1	8.5	0	1	0
1 < 2	10.5	47.0	1	4.5
2 < 3	12.6	54.5	1	4.3
3 < 4	14.6	58.1	1	4
4 < 5	16.4	58.5	1	3.6
5 < 6	18.8	60.1	1	3.2
6 < 7	21.0	21.0	1	1
7 < 8	23.5	21.0	1	0.89
8 < 9	27.3	21.0	1	0.77
9 < 10	29.6	21.0	1	0.71
10 < 11	34.3	21.0	1	0.61
11 < 12	40.0	21.0	1	0.53
12 < 13	45.2	21.0	1	0.46
13 < 14	48.6	21.0	1	0.43
14 < 15	52.8	21.0	1	0.40
15 < 16	53.9	21.0	1	0.39
16 < 17	55.3	21.0	1	0.38
17 < 18	58.3	21.0	1	0.36
18 < 25	57.1	21.0	7	2.6
25 < 30	59.9	21.0	5	1.8
<p>1 - 50th percentile body weights taken from U.S. EPA, 1989b, pp. 5-43 & 5-45.</p> <p>2 - Soil Ingestion Rate calculated in Table 8-3.</p> <p>3 - Weighting Factor is equal to the number of years represented by each age group.</p> <p>4 - The Soil Ingestion Rate Normalized to Body Weight for the specified time period.</p> <p>Example Calculation, age 1 < 2: $[(47.0 \text{ mg soil/d}) * 1 \text{ yr}]/10.5 \text{ kg} = 4.5 \text{ (mg * yr)/(kg * d)}$ </p>				

STEP 4: Finally, these age-specific values are combined to yield the time-weighted, normalized values used in the *ShortForm* for the subchronic, chronic and 30-year exposures. These values are developed in Table 8-5, and the results summarized in Table 8-1.

TABLE 8-5

CALCULATION OF THE NORMALIZED DAILY SOIL INTAKE RATES USED IN THE RESIDENTIAL SHORTFORM			
SUBCHRONIC EXPOSURE AGE years		DAILY SOIL INGESTION RATE FOR THE TIME PERIOD (mg * yrs)/(kg * d)	
1 < 2 # Years = 1		4.5 ----- SUM: 4.5	
Normalized Average Daily Soil Intake Rate: $4.5/1 = 4.5 \text{ mg soil}/(\text{kg} \cdot \text{day})$			
CHRONIC EXPOSURE AGE years		DAILY SOIL INGESTION RATE FOR THE TIME PERIOD (mg * yrs)/(kg * d)	
1 < 2 2 < 3 3 < 4 4 < 5 5 < 6 6 < 7 7 < 8		4.5 4.3 4 3.6 3.2 1 0.89	
# Years = 7		----- SUM: 21.5	
Normalized Average Daily Soil Intake Rate: $21.5/7 = 3.1 \text{ mg soil}/(\text{kg} \cdot \text{day})$			
		30 YEAR EXPOSURE AGE years	
		DAILY SOIL INGESTION RATE FOR THE TIME PERIOD (mg * yrs)/(kg * d)	
		< 1 1 < 2 2 < 3 3 < 4 4 < 5 5 < 6 6 < 7 7 < 8 8 < 9 9 < 10 10 < 11 11 < 12 12 < 13 13 < 14 14 < 15 15 < 16 16 < 17 17 < 18 18 < 25 25 < 30	
		0 4.5 4.3 4 3.6 3.2 1 0.89 0.77 0.71 0.61 0.53 0.46 0.43 0.40 0.39 0.38 0.36 2.6 1.8	
		----- Exposure Period = 30 yr SUM: 31	
		AVERAGING PERIOD 75 Years	
Normalized Lifetime Average Daily Soil Intake Rate: $31/75 = 0.41 \text{ mg soil}/(\text{kg} \cdot \text{day})$			
For the evaluation of non-cancer risk, the averaging period is equal to the exposure period. For cancer risk, the averaging period is a lifetime (75 years), independent of the length of the exposure period (MA DEQE, 1989a).			

8.7.3 Dermal Contact Rates

This section will describe the development of the rates of contact between the soil and the receptor's skin. Absorption through the skin is potentially an important route of exposure which depends, in part, on the exposed skin surface area. Since surface area varies by age, the soil/dermal contact rate would be expected to vary by age as well. The rates developed in a step-wise fashion in the following tables are embedded in the *ShortForm* formulae. The values are age-specific and are normalized to body weight. The exposure model used to quantify the dermal contact exposure pathway assumes that some contact will occur in the home during winter months, but that the majority of the exposure will be received from indoor and outdoor exposures during the warmer time of the year. As a result of the detailed analysis, each age group experiences a slightly different exposure, and annual average daily contact rates calculated range between 10 to 1200 mg of soil per day. The step-wise process followed in the calculation of the exposure rates is summarized below and detailed in Tables 8-6 through 8-10.

- STEP 1:** For exposures which occur indoors, the amount of soil which comes into contact with the receptor's skin is calculated in Table 8-6. This contact rate is for those days when exposure is thought to occur. The indoor exposure is quantified for ages 0 - 6. During the colder months only the hands are assumed to be regularly exposed to household dust, and infants are assumed not to be exposed. During the warmer months children are assumed to have a greater surface area exposed. The amount of soil in contact with the skin is dependent upon the surface area of the exposed body parts, the adherence of the dust to the skin, and the fraction of the household dust derived from soil sources.
- STEP 2:** For the days when the receptor is exposed both indoors and outdoors, the amount soil in contact is calculated in Table 8-7. This contact rate is for those days when exposure is thought to occur. Exposure to adults is quantified here as it is assumed that all ages have the opportunity for contact with the soil through play or gardening.
- STEP 3:** The indoor and outdoor soil contact rates (the results of Tables 8-6 and 8-7, respectively) are then combined with exposure frequency assumptions to yield an average daily soil contact rate for the year. These rates are presented in Table 8-8, and range between 10 to 1200 mg soil per day, depending upon the age of the receptor.

TABLE 8-6

INDOORS ONLY - DERMAL CONTACT

OCTOBER - APRIL

AGE years	Exposed Body Parts and % of Total Body Surface Area ¹	Total Body Surface Area ² cm ²	Adherence Factor ³ mg/cm ²	Fraction of Dust Derived From Soil ⁴	Soil In Contact With Skin On Days Exposed INDOORS ONLY ⁵ mg soil/day
< 1	none, -	4450 ⁶	0.056	0.8	-
1 < 2	hands, 5.68%	5130 ⁶	0.056	0.8	13.1
2 < 3	hands, 5.3%	5790	0.056	0.8	13.7
3 < 4	hands, 6.1%	6490	0.056	0.8	17.7
4 < 5	hands, 5.7%	7060	0.056	0.8	18.0
5 < 6	hands, 5.7%	7790	0.056	0.8	19.9
> 6	none, -	-	0.056	0.8	-

MAY - SEPTEMBER

AGE years	Exposed Body Parts and % of Total Body Surface Area	Total Body Surface Area ² cm ²	Adherence Factor ³ mg/cm ²	Fraction of Dust Derived From Soil ⁴	Soil In Contact With Skin On Days Exposed INDOORS ONLY ⁵ mg soil/day
< 1	Hands, Arms, Legs, Feet, 46%	4450	0.056	0.8	91.7
1 < 2	Hands, Arms, Legs, Feet, 48%	5130	0.056	0.8	110.3
2 < 3	Hands, Arms, Legs, Feet, 47%	5790	0.056	0.8	121.9
3 < 4	Hands, Arms, Legs, Feet, 54%	6490	0.056	0.8	157.0
4 < 5	Hands, Arms, Legs, Feet, 55%	7060	0.056	0.8	174.0
5 < 6	Hands, Arms, Legs, Feet, 52% ⁷	7790	0.056	0.8	181.5
> 6	none, -	-	0.056	0.8	-

- 1 - Percentage of total body surface area by body part taken from U.S. EPA, 1989b, (mean values, p.4-12).
- 2 - 50th Percentile values for Total Body Surface Areas taken from U.S. EPA, 1989b (p. 4-31), except as noted below (6).
- 3 - Hawley, 1985
- 4 - Hawley, 1985
- 5 - The soil in contact with the skin (on days exposed) during this time period for the age group specified.
Example calculation, age <1: $0.46 * 4450 * 0.056 * 0.8 = 91.7$ mg soil
- 6 - The total body surface area for ages <1 and 1<2 have been estimated using the equation $SA = K * BW^{2/3}$ (U.S. EPA, 1989b, p. 4-20), where SA = Surface Area, K is a constant (estimated from data available for ages 2<3) and BW is the receptor's body weight (Table 8-8).
- 7 - Data are unavailable for this age group. The Percentage of total body surface area used here is assumed to be equal to that for the 6 > 7 year old.

TABLE 8-7

INDOORS & OUTDOORS - DERMAL CONTACT

MAY - SEPTEMBER

AGE years	Exposed Body Parts and % of Total Body Surface Area ¹	Total Body Surface Area ² cm ²	Adherence Factor ³ mg/cm ²	Fraction Adhered Material Derived from Soil ⁴	Soil In Contact With Skin On Days Exposed Both Indoors & Outdoors ⁵ mg soil/day
< 1	none, -	4450 ⁶	0.51	0.8	0
1 < 2	Hands, Arms, Legs, Feet, 48%	5130 ⁶	0.51	0.8	1005
2 < 3	Hands, Arms, Legs, Feet, 47%	5790	0.51	0.8	1110
3 < 4	Hands, Arms, Legs, Feet, 54%	6490	0.51	0.8	1430
4 < 5	Hands, Arms, Legs, Feet, 55%	7060	0.51	0.8	1584
5 < 6	Hands, Arms, Legs, Feet, 52% ⁷	7790	0.51	0.8	1653
6 < 7	Hands, Arms, Legs, Feet, 52%	8430	0.51	0.8	1789
7 < 8	Hands, Arms, Legs, Feet, 54% ⁷	9170	0.51	0.8	2020
8 < 9	Hands, Arms, Legs, Feet, 54% ⁷	10000	0.51	0.8	2203
9 < 10	Hands, Arms, Legs, Feet, 54%	10600	0.51	0.8	2335
10 < 11	Hands, Arms, Legs, Feet, 57% ⁷	11700	0.51	0.8	2721
11 < 12	Hands, Arms, Legs, Feet, 57% ⁷	13000	0.51	0.8	3023
12 < 13	Hands, Arms, Legs, Feet, 57%	14000	0.51	0.8	3256
13 < 14	Hands, Arms, Legs, Feet, 57%	14800	0.51	0.8	3442
14 < 15	Hands, Arms, Legs, Feet, 59% ⁷	15500	0.51	0.8	3731
15 < 16	Hands, Arms, Legs, Feet, 59% ⁷	15700	0.51	0.8	3779
16 < 17	Hands, Arms, Legs, Feet, 59%	16000	0.51	0.8	3852
17 < 18	Hands, Arms, Legs, Feet, 61%	16300	0.51	0.8	4057
18 < 30	Hands, Forearms, Lower legs, Feet, 30%	16900	0.51	0.8	2069
<p>1 - Mean values for Percentage of total body surface area by body part taken from U.S. EPA, 1989b (pp. 4-11 & 4-12), except as noted below (7).</p> <p>2 - 50th Percentile Total Body Surface Areas taken from U.S. EPA, 1989b (pp. 4-29 & 4-31), except as noted below (6).</p> <p>3 - Hawley, 1985</p> <p>4 - Hawley, 1985</p> <p>5 - The soil in contact with the skin (on days exposed) during this time period for the age group specified. Example calculation, age 1 < 2: $0.48 * 5130 * 0.51 * 0.8 = 1005 \text{ mg soil/day}$</p> <p>6 - The total body surface area for ages <1 and 1<2 have been estimated using the equation $SA = K * BW^{2/3}$ (U.S. EPA, 1989b, p. 4-20), where SA = Surface Area, K is a constant (estimated from data available for ages 2<3) and BW is the receptor's body weight (Table 8-8).</p> <p>7 - Data are unavailable for this age group. The Percentage of total body surface area used here is taken from the next oldest age group for which data is available (i.e., the % for the 6<7 yr old is used for the 5<6 age group).</p>					

TABLE 8-8

CALCULATION OF AGE-SPECIFIC SOIL DERMAL CONTACT RATES

AGE years	SOIL DERMAL CONTACT RATES ** On days exposed **			FREQUENCY OF EXPOSURE			ANNUAL AVERAGE 365 days
	Indoor Only Oct -> April ¹	Indoor Only May -> Sept. ²	Indoor & Outdoor May -> Sept. ³	Indoor Only Oct -> April ⁴ of 212 days	Indoor Only May -> Sept. ⁵ of 153 days	Indoor & Outdoor May -> Sept. ⁶ of 153 days	DAILY SOIL DERMAL CONTACT RATE ⁷ mg soil/d
	mg soil/day	mg soil/day	mg soil/day	days	days	days	
< 1	0	91.7	0	0	44	0	11.1
1 < 2	13.1	110.3	1005	212	44	109	321
2 < 3	13.7	121.9	1110	212	44	109	354
3 < 4	17.7	157.0	1430	212	44	109	456
4 < 5	18.0	174.0	1584	212	44	109	504
5 < 6	19.9	181.5	1653	212	44	109	527
6 < 7	0	0	1789	0	0	109	534
7 < 8	0	0	2020	0	0	109	603
8 < 9	0	0	2203	0	0	109	658
9 < 10	0	0	2335	0	0	109	697
10 < 11	0	0	2721	0	0	109	813
11 < 12	0	0	3023	0	0	109	903
12 < 13	0	0	3256	0	0	109	972
13 < 14	0	0	3442	0	0	109	1028
14 < 15	0	0	3731	0	0	109	1114
15 < 16	0	0	3779	0	0	109	1129
16 < 17	0	0	3852	0	0	109	1150
17 < 18	0	0	4057	0	0	109	1212
18 < 30	0	0	2069	0	0	109	618

- 1 - Indoor Only Contact Rates for October through April taken from Table 8-6.
 2 - Indoor Only Contact Rates for May through September taken from Table 8-6.
 3 - Contact Rates on days when both indoor and outdoor exposure is thought to occur taken from Table 8-7.
 4 - 212 days is approximately 7 days/week from October through April.
 5 - 44 days is approximately 2 days/week from May through September.
 6 - 109 days is approximately 5 days/week from May through September.
 7 - The average daily exposure to soil in dermal contact with the skin for this age group, adjusted for the frequency of exposure. Example calculation, age 2<3 years:

$$((13.7 * 212) + (121.9 * 44) + (1110 * 109))/365 = 354 \text{ mg soil/day}$$

STEP 4: The annual average contact rates derived in Table 8-8 are then normalized to the body weight of each age group and weighted by the number of years in that age group. This calculation is presented in Table 8-9.

TABLE 8-9

CALCULATION OF TIME-WEIGHTED AVERAGE DAILY SOIL DERMAL CONTACT EXPOSURES NORMALIZED TO BODYWEIGHT				
AGE	MEDIAN BODY WEIGHT ¹	SOIL DERMAL CONTACT RATE ²	WEIGHTING FACTOR ³	DAILY SOIL DERMAL CONTACT RATE FOR THE TIME PERIOD ⁴
years	kilograms	mg soil/day	years	(mg * yrs)/(kg * d)
< 1	8.5	11.1	1	1.3
1 < 2	10.5	321	1	30.6
2 < 3	12.6	354	1	28.1
3 < 4	14.6	456	1	31.2
4 < 5	16.4	504	1	30.7
5 < 6	18.8	527	1	28.0
6 < 7	21.0	534	1	25.4
7 < 8	23.5	603	1	25.7
8 < 9	27.3	658	1	24.1
9 < 10	29.6	697	1	23.5
10 < 11	34.3	813	1	23.7
11 < 12	40.0	903	1	22.6
12 < 13	45.2	972	1	21.5
13 < 14	48.6	1028	1	21.2
14 < 15	52.8	1114	1	21.1
15 < 16	53.9	1129	1	20.9
16 < 17	55.3	1150	1	20.8
17 < 18	58.3	1212	1	20.8
18 < 25	57.1	618	7	75.8
25 < 30	59.9	618	5	51.6

1 - 50th percentile body weights taken from U.S. EPA, 1989b, pp. 5-43 & 5-45.
 2 - Soil Dermal Contact calculated in Table 8-8.
 3 - Weighting Factor is equal to the number of years represented by each age group.
 4 - The Soil Dermal Contact Rate Normalized to Body Weight for the specified time period. Example Calculation, age 1 < 2:

$$[(321 \text{ mg soil/d}) * 1 \text{ yr}] / 10.5 \text{ kg} = 30.6 \text{ (mg * yr)/(kg * d)}$$

STEP 5: Finally, these age-specific values are combined to yield the time-weighted, normalized exposure rates used in the *ShortForm* for the subchronic, chronic and 30-year exposures. These values are developed in Table 8-10 and the results summarized in Table 8-1.

TABLE 8-10

CALCULATION OF THE NORMALIZED DAILY SOIL DERMAL CONTACT RATES USED IN THE RESIDENTIAL SHORTFORM

SUBCHRONIC EXPOSURE	DAILY SOIL DERMAL CONTACT RATE FOR THE TIME PERIOD
AGE years	(mg * yrs)/(kg * d)
1 < 2	30.6
# Years = 1	SUM: 30.6
Normalized Average Daily Soil Dermal Contact Rate:	
30.6/1 = 30.6 mg soil/(kg*day)	

CHRONIC EXPOSURE	DAILY SOIL DERMAL CONTACT RATE FOR THE TIME PERIOD
AGE years	(mg * yrs)/(kg * d)
1 < 2	30.6
2 < 3	28.1
3 < 4	31.2
4 < 5	30.7
5 < 6	28.0
6 < 7	25.4
7 < 8	25.7
# Years = 7	SUM: 199.7
Normalized Average Daily Soil Dermal Contact Rate:	
199.7/7 = 28.5 mg soil/(kg*day)	

30 YEAR EXPOSURE	DAILY SOIL DERMAL CONTACT RATE FOR THE TIME PERIOD
AGE years	(mg * yrs)/(kg * d)
< 1	1.3
1 < 2	30.6
2 < 3	28.1
3 < 4	31.2
4 < 5	30.7
5 < 6	28.0
6 < 7	25.4
7 < 8	25.7
8 < 9	24.1
9 < 10	23.5
10 < 11	23.7
11 < 12	22.6
12 < 13	21.5
13 < 14	21.2
14 < 15	21.1
15 < 16	20.9
16 < 17	20.8
17 < 18	20.8
18 < 25	75.8
25 < 30	51.6
Exposure Period = 30 yr	SUM: 548.6
AVERAGING PERIOD	
75 Years	
Normalized Lifetime Average Daily Soil Dermal Contact Rate:	
548.6/75 = 7.3 mg soil/(kg * day)	

For the evaluation of non-cancer risk, the averaging period is equal to the exposure period. For cancer risk, the averaging period is a lifetime (75 years), independent of the length of the exposure period (MA DEQE, 1989a).

8.8 Soil Particulates - Inhalation

The *Risk Assessment ShortForm - Residential Scenario* does not include a quantification of potential risks associated with the inhalation of fugitive dust at or from a disposal site.

8.8.1 Discussion Of Pathway

The inhalation of fugitive dust (airborne soil particulates) is a potential exposure pathway which is frequently included for disposal sites where surficial soil contamination is present.

Typically, neither the analysis of fugitive dust for oil or hazardous materials (OHM) nor monitoring of suspended particulate levels are performed during the site investigation and the risk assessor is left to construct a hypothetical model to quantify potential risks. Pathway-specific assumptions are made about: (1) the level of particulates in the air, (2) the concentration of OHM in the fugitive dust, (3) the percentage of dust in the ambient air derived from the site soil, (4) the volume of dust-laden soil inhaled by a receptor and (5) the amount of OHM which may dissociate from the soil particles and be absorbed by the human body.

The *Residential ShortForm* acknowledges that the residential receptors may be exposed to oil or hazardous materials via direct contact with contaminated surficial soils (see Section 8.7) and via the inhalation of soil-derived suspended particulates in air.

However, for residential (non-construction) exposure scenarios, the exposure to OHM via the fugitive dust pathway is insignificant relative to the direct contact exposures. For this reason the fugitive dust pathway is not quantified in the Residential ShortForm.

A demonstration of the insignificance of this pathway for a residential exposure scenario is presented in the following sections. Overall, a receptor's lifetime exposure to fugitive dust may represent only one one-hundredth of 1 percent (0.01 %) of the exposure received via incidental ingestion and dermal contact.

This pathway may be of greater importance (and should be quantified) at disposal sites where:

- there are large areas of exposed (i.e. no vegetative ground cover) contaminated surficial soil,
- the current or foreseeable future use of the property includes excavation/construction activities,
- there are demonstrably high levels of fugitive dust in the air,
- inhalation of fugitive dust is the only potential exposure pathway for the soil, or
- the chemicals of concern are known to be relatively more toxic (by two+ orders of magnitude) via inhalation than by ingestion or dermal absorption.

8.8.2 Demonstration Of Insignificance

The following tables were generated based upon information from the soil exposure summary spreadsheets prepared by the MA DEP Office of Research and Standards (MA DEP, 1991a). The average daily intake rates which appear in the tables are time-weighted averages which are normalized to body weight ($\text{mg}_{\text{soil}}/\text{kg}_{\text{body weight}}/\text{day}$). The calculations for soil ingestion and dermal contact exposure estimates are in more detail in Section 8.7. The equation for the calculation of potential exposure via the inhalation of particulates is given in the next section. The (conservative) assumption was made that the concentration of soil respirable particulates is the same indoors and outdoors.

Table 8-11 compares the age specific receptor exposure via the inhalation of particulates to the receptors concurrent exposure via incidental ingestion. For those receptors with a higher tendency to ingest soil (young children aged 1-6 years) the inhalation/(inhalation + ingestion) ratio ranges as low as 0.0008 (0.08 %, age 2-3 years). The highest ratio (0.006, 0.6%) for ages greater than 18 years old) indicates that the particulate contribution to exposure is still just a fraction (< 1%) of the exposure attributable to incidental soil ingestion.

TABLE 8-11

COMPARISON OF INHALATION OF PARTICULATES TO SOIL INGESTION PATHWAY

Age years	Average Daily Soil Particulate Inhalation Rate ¹ mg _{soil} /kg/day	Daily Soil Ingestion Rate ² mg _{soil} /kg/day	% of Combined Exposure (Inh. & Ing.) Attributable to Inhaled Particulates ³
1-2	0.0041	4.5	0.09 %
2-3	0.0035	4.3	0.08 %
3-4	0.0038	4	0.09 %
4-5	0.004	3.6	0.1 %
5-6	0.0035	3.2	0.1 %
6-7	0.0023	1	0.2 %
7-8	0.0029	0.89	0.3 %
8-9	0.0025	0.77	0.3 %
9- 10	0.0023	0.71	0.3 %
10-11	0.002	0.61	0.3 %
11-12	0.0017	0.53	0.3 %
12-13	0.0024	0.46	0.5 %
13-14	0.0023	0.43	0.5 %
14-15	0.0021	0.40	0.5 %
15-16	0.002	0.39	0.5 %
16-17	0.002	0.38	0.5 %
17-18	0.0019	0.36	0.5 %
18-25	0.0026	2.6/7 = 0.4	0.6 %
25-30	0.0024	1.8/5 = 0.4	0.6 %
<hr/>			
MEAN age 1-2:	0.0041 mg _{soil} /kg/d	4.5 mg _{soil} /kg/d	0.09 %
MEAN ages 1-8:	0.0034 mg _{soil} /kg/d	3.1 mg _{soil} /kg/d	0.1 %
MEAN ages 1-30:	0.0026 mg _{soil} /kg/d	1.1 mg _{soil} /kg/d	0.2 %

- 1 - Average Daily Soil Particulate Inhalation Rate calculated from equation in Section 8.8.3.
 2 - Daily Soil Ingestion Rate from Table 8-4.
 3 - (Column 2/(Column 2 + Column 3)) * 100. Example Calculation, ages 25-30:

$$(0.0024/(0.0024 + 0.4)) * 100 = 0.6 \%$$

Table 8-12 presents a similar analysis, comparing the particulate inhalation exposures to those received via dermal contact with the contaminated soils. Once again the exposure attributable to the inhalation of particulates is relatively insignificant, perhaps as high as 0.02 % of the dermal exposure for some age groups.

TABLE 8-12

COMPARISON OF INHALATION OF PARTICULATES TO SOIL DERMAL CONTACT PATHWAY			
Age	Average Daily Soil Particulate Inhalation Rate¹	Daily Soil Dermal Contact Rate²	% of Combined Exposure (Inh. & Derm.) Attributable to Inhaled Particulates³
years	mg_{soil}/kg/day	mg_{soil}/kg/day	
1-2	0.0041	30.6	0.01 %
2-3	0.0035	28.1	0.01 %
3-4	0.0038	31.2	0.01 %
4-5	0.004	30.7	0.01 %
5-6	0.0035	28.0	0.01 %
6-7	0.0023	25.4	0.01 %
7-8	0.0029	25.7	0.01 %
8-9	0.0025	24.1	0.01 %
9-10	0.0023	23.5	0.01 %
10-11	0.002	23.7	0.01 %
11-12	0.0017	22.6	0.01 %
12-13	0.0024	21.5	0.01 %
13-14	0.0023	21.2	0.01 %
14-15	0.0021	21.1	0.01 %
15-16	0.002	20.9	0.01 %
16-17	0.002	20.8	0.01 %
17-18	0.0019	20.8	0.01 %
18-25	0.0026	75.8/7 = 10.8	0.02 %
25-30	0.0024	51.6/5 = 10.3	0.02 %
-----	-----	-----	-----
MEAN age 1-2:	0.0041 mg _{soil} /kg/d	30.6 mg _{soil} /kg/d	0.01 %
MEAN ages 1-8:	0.0034 mg _{soil} /kg/d	28.5 mg _{soil} /kg/d	0.01 %
MEAN ages 1-30:	0.0026 mg _{soil} /kg/d	18.9 mg _{soil} /kg/d	0.01 %
1 - Average Daily Soil Particulate Inhalation Rate calculated from equation in Section 8.8.3. 2 - Daily Soil Dermal Contact Rate from Table 8-9. 3 - (Column 2/(Column 2 + Column 3)) * 100. Example Calculation, ages 25-30: (0.0024/(0.0024 + 10.3)) * 100 = 0.02 %			

Table 8-13 summarizes the relationship between the estimated exposure from the inhalation of fugitive dust and the exposure received from direct contact (incidental ingestion and dermal contact combined) with the contaminated surficial soil.

TABLE 8-13

**INHALATION PATHWAY EXPOSURE
AS A PERCENTAGE OF TOTAL
(INGESTION & DERMAL) SOIL EXPOSURE**

Receptor (age in years)	Ratio of Inhaled Particulate Exposure to Total (Ingestion + Dermal + Inhalation) Exposure %
MEAN, 1 - 2 years	0.01 %
MEAN, 1 - 8 years	0.01 %
MEAN, 1 - 30 years	0.01 %

NOTE: This demonstration of the relative insignificance of exposure via the inhalation of particulates does not consider the absorption efficiencies of specific chemicals, nor the relative importance of chemicals exhibit toxic effects at the portal of entry. Chemical-specific information can and should be used to evaluate specific circumstances. The conclusions drawn here should be interpreted as a gross generalization.

8.8.3 Equations

The equation used to evaluate potential exposure associated with inhalation of contaminated airborne particulates is given as:

$$ADE_{\text{soil, 1 year}} = E_{\text{winter}} + E_{\text{spring\&fall}} + E_{\text{summer}} \quad (3)$$

and

$$E_{\text{soil, seasonal}} = \frac{[RP]_{\text{air}} * P * VR * F * D1 * D2 * C * DE}{BW * AP} \quad (4)$$

Where:

$[ADE]_{\text{soil, 1 year}} =$	The <u>A</u> verage <u>D</u> aily <u>E</u> xposure to airborne <u>soil</u> particulates in air (calculated for 1 year: winter, spring & fall, and summer). In units: mg/kg/day.
$E =$	Seasonal exposures (winter, spring & fall, and summer), each averaged over the year. In units: mg/kg/day.
$P =$	The <u>P</u> roportion (fraction) of the respirable particulate assumed to be derived from the contaminated on-site soils. Dimensionless.
$[RP]_{\text{air}} =$	The concentration of <u>R</u> espirable <u>P</u> articulates (PM10) in air. In units: $\mu\text{g}/\text{m}^3$.
$VR =$	Respiratory rate for the receptor of concern. In units: m^3/hour .
$F =$	The <u>F</u> requency (F) of exposure. In units: events/day.
$D1 =$	The <u>D</u> uration (D1) of each exposure event. In units: hours/event.
$C =$	Units <u>C</u> onversion factor: $10^{-3} \text{ mg}/\mu\text{g}$.
$D2 =$	The <u>D</u> uration (D2) of the exposure period. In units: days.
$DE =$	Deposition Efficiency of PM10 in lung. In units: percent
$BW =$	The receptor's <u>B</u> ody <u>W</u> eight. In units: kg.
$AP =$	The <u>A</u> veraging <u>P</u> eriod (AP). In units: days.

TABLE 8-14

INHALATION OF PARTICULATES - EXPOSURE ASSUMPTIONS

Parameter	Value or Range of Values	Discussion
Respirable Particulate Concentration, [RP] _{air}	44 $\mu\text{g}/\text{m}^3$	The maximum annual <u>mean</u> recorded PM ₁₀ level in Massachusetts in 1986 (MA DEQE, 1987)
Proportion, P	0.4 or 0.5	In the winter, 40% (0.4) of the fugitive dust in the air is assumed to come from the local (contaminated) area. In the spring, summer and fall 50% (0.5) of the respirable particulates are assumed to have the contaminated area as their source.
Respiratory Volume, VR	0.17 - 1.04 m^3/hr	Hourly intake for the receptor of concern: age specific. (U.S. EPA, 1989b)
Frequency of Exposure, F	1 event/day	The receptors are assumed to spend at least part of every day in the home, and thus exposed to the contaminated fugitive dust.
Duration of Exposure Event, D1	24 hr/event 12 hr/event 16 hr/event	<ul style="list-style-type: none"> - Children 0-6 years are assumed to spend 24 hr/day at home, as are children 6-12 years during the summer. - Children 6-18 years are assumed to spend 12 hr/day at home during the fall, winter and spring months, as are children 12-18 yrs during the summer. - Female adults are assumed to spend 16 hr/day at home.
Duration of Exposure Period, D2	92, 122, or 151 days	WINTER: 151 days, Nov. -> March SPRING & FALL: 122 days, April, May, September & October SUMMER: 92 days, June, July & August
Averaging Period, AP	365 days	365 days per year of exposure for the indicated receptor
Body Weight, BW	10.8 to 59.9 kg	Age-specific values, ranging from 8.5 kg for a child < 1 yr to 59.9 kg for a 3-year old female (US EPA, 1989b)
Deposition Efficiency	50 %	50 th percentile female (MA DEP, 1991a; US EPA, 1989b)

8.9 Drinking Water - Inhalation, Dermal Contact, and Ingestion

8.9.1 Narrative Description

The *Residential ShortForm* evaluation of drinking water includes consideration of three potential exposure routes which may result from the use of contaminated water: (1) *inhalation* of substances volatilized from the water; (2) *dermal absorption* of chemicals during skin contact with the water; and (3) *ingestion* of the contaminated drinking water. Inhalation and dermal exposures would typically occur during showering, bathing, washing dishes, cooking, and other household activities.

The residential receptor is not assumed to be exposed to all chemicals via all three exposure routes. Those substances which are considered to be *volatile organic compounds* (or VOCs) are evaluated for all three exposure routes. *Semi-volatile organic compounds* (or SVOCs) are evaluated for dermal and ingestion exposures. Metals are evaluated for ingestion exposures only.

For volatile organic compounds, it is assumed that inhalation exposures resulting from the use of contaminated drinking water may result in absorbed doses and risks equal to or greater than the ingestion doses and risks associated with drinking the water (Andelman, 1985; Foster and Chrostowski, 1987; McKone, 1987; McKone, 1991a). For dermally absorbed compounds (VOCs and SVOCs), it has also been suggested that doses received via dermal contact during bathing or showering may be equal to or greater than the doses associated with ingestion exposures (Brown, 1984). This analysis thus assumes that exposures associated with inhalation and dermal contact are each equal to those estimated from drinking the contaminated water. [These assumptions are being re-evaluated by the Department, and future versions of the *Residential ShortForm* may use a different model.]

For **VOCs**, the total dose and total risk associated with exposure to contaminated drinking water is three times the dose and risk associated with drinking the water *only*.

For **SVOCs**, the total dose and risk associated with exposure to contaminated drinking water is twice the dose and risk associated with drinking the water *only*.

For **metals**, the total dose associated with exposure to contaminated drinking water is equal to the dose associated with drinking the water *only*.

The *Residential ShortForm* estimates exposures associated with subchronic, chronic and 30 year (adult) exposures. Note that the 30 year exposure is assumed to occur entirely during adulthood to be consistent with standard US EPA and MA DEP practices for evaluating drinking water exposures. A lifetime average body weight (62 kg) is used with an adult drinking water intake (2 liters/day), rather than weighted averages over the 0-30 year age period. This simplification is considered justified since water intake increases with age, and the dose remains relatively constant over a lifetime. This trend is shown in Figure 8-2, where the intake normalized to bodyweight for ages 0 to 18, while variable, averages to approximately the adult exposure.

8.9.2 Equations

The equation used to evaluate potential *non-carcinogenic* effects associated with exposure to contaminated drinking water is given as:

$$HI = \frac{[OHM]_{dw} * VI * RAF * F * D1 * D2 * MULT}{RfD * BW * AP * C} \quad (5)$$

The equation used to evaluate potential *carcinogenic* effects associated with exposure to contaminated drinking water is given as:

$$ELCR = \frac{[OHM]_{dw} * VI * RAF * F * D1 * D2 * MULT * CPV}{BW * AP * C} \quad (6)$$

Where the exposure related terms (not shaded above) are:

$[OHM]_{dw}$ = The Operational Exposure Point Concentration (EPC) of the oil or hazardous material in drinking water. In units: $\mu\text{g/liter}$.

VI = Daily volume of drinking water ingested by the receptor of concern. In units: liters/day.

RAF = The Relative Absorption Factor for drinking water ingestion and threshold effects (A chemical- and route- specific value). Dimensionless.

F and D1 = The Frequency (F) of exposure and the Duration (D1) of each exposure event. The receptors are assumed to be exposed to the drinking water each and every day, and that exposure occurs over the course of the day.
 $F = 1 \text{ event/day}$ and $D1 = 1 \text{ day/event}$
 The product of these terms is equal to 1, and it is dimensionless. They have thus been eliminated from the actual formulae contained in the spreadsheet.

D2 and AP = The Duration (D2) of the exposure period and the Averaging Period (AP). For the purposes of these evaluations, the drinking water exposures are assumed to occur over the relevant age of the receptor:

Subchronic:	D2 = 1 year	AP = 1 year
Chronic:	D2 = 7 years	AP = 7 years
Lifetime:	D2 = 30 years	AP = 75 years

The quotient of these two terms is dimensionless.

MULT = The Multiplier for non-ingestion in-home uses of the water. Dimensionless.

BW = The receptor's Body Weight, age specific. In units: kg.

C = Units Conversion Factor: $10^3 \mu\text{g/mg}$.

8.9.3 Summary of Drinking Water Exposure Parameters

TABLE 8-15

DRINKING WATER - EXPOSURE ASSUMPTIONS			
Parameter	for Subchronic HI Calculations	for Chronic HI Calculations	for ELCR Calculations
Water Volume Ingested, VI	1 liter/day Discussion follows	1 liter/day Discussion follows	2 liters/day Discussion follows
Relative Absorption Factor, RAF	0.006 - 1.3 Discussion follows	0.006 - 1.3 Discussion follows	0.006 - 1.3 Discussion follows
Multiplier, MULT	1, 2, or 3 Discussion follows	1, 2, or 3 Discussion follows	1, 2, or 3 Discussion follows
Body Weight, BW	10.5 kg Discussion follows	16.8 kg Discussion follows	62 kg Discussion follows
Frequency of Exposure, F	1 event/day Each day is considered an exposure "event"	1 event/day Each day is considered an exposure "event"	1 event/day Each day is considered an exposure "event"
Duration of Exposure Event, D1	1 day/event The consumption of water is assumed to take place over the course of the day	1 day/event The consumption of water is assumed to take place over the course of the day	1 day/event The consumption of water is assumed to take place over the course of the day
Duration of Exposure Period, D2	1 year The drinking water is assumed to remain contaminated over the course of the 1 year subchronic exposure	7 years The drinking water is assumed to remain contaminated over the course of the 7 year chronic exposure	30 years The drinking water is assumed to remain contaminated over the duration of the residential period
Averaging Period, AP	1 year For the evaluation of noncarcinogenic effects, AP = D2	7 years For the evaluation of noncarcinogenic effects, AP = D2	75 years For the evaluation of carcinogenic effects, the AP is equal to a lifetime

8.9.4 Exposure Parameters

There are four exposure parameters in the equations which evaluate drinking water related exposures. The input value for each parameter may vary according to the type of risk being evaluated (carcinogenic or non-carcinogenic) and the chemical of concern. Each of the parameters are discussed in more detail below.

8.9.4.1 Water Volume Ingested, VI

The drinking water consumption rates of 2 liters/day for adult (lifetime) exposures and 1 liter/day for infant's (subchronic) and childhood (chronic) exposures are standard assumptions described by the U.S. Environmental Protection Agency (U.S. EPA 1989b & 1991). An individual's water intake may vary by age, sex, geography or level of activity. Estimates of mean tap water consumption rates for adults (of various ages) fall in the range of approximately 0.6 to 1.6 liters/day. Estimates of mean intakes for young children fall in the range of approximately 0.2 to 0.5 liters/day (Ershow and Cantor, 1989).

8.9.4.2 Body Weight, BW

For each receptor evaluated, the values chosen represents the 50th percentile of the female body weight for the age group under consideration (US EPA, 1989b).

Female, age 1-2 years,	BW = 10.5 kg
Female, age 1-8 years,	BW = 16.8 kg
Female, adult lifetime,	BW = 62 kg

These values are embedded in the formulae contained in the spreadsheet.

8.9.4.3 Relative Absorption Factor, RAF

The methodology for deriving these chemical- and route-specific factors has been described by both the MA DEP and the U.S. EPA (MA DEQE, 1989a; US EPA, 1989a). The derivation of the input values used in this spreadsheet may be found in Appendix C. It should be remembered that an RAF is not simply an absorption factor.

8.9.4.4 Multiplier, MULT

Multipliers are used to evaluate potential exposures to a residential receptor from dermal contact with contaminated drinking water and the inhalation of material volatilized from the water. Various papers (Andelman, 1985; Brown, 1984) have indicated that the exposures received via each of these pathways may be roughly approximate to the dose from ingesting the water. A Multiplier of three (3) is used for chemicals which may be dermally absorbed, inhaled and ingested. A multiplier of two (2) is used for chemicals which may be dermally absorbed and ingested. A Multiplier of one (1) is used for chemicals which are not volatile nor easily absorbed through the skin.

The assumption of equivalency between exposure pathways related to drinking water is being examined by the Department, and alternative models may be incorporated into future versions of the *ShortForm*.

TABLE 8-16

CHEMICALS AND THEIR ASSIGNED DRINKING WATER USAGE MULTIPLIERS		
1	2	3
Arsenic Cadmium Chromium Lead Nickel Silver Thallium Zinc	Bis(2-ethylhexyl)phthalate Cyanide Mercury PAHs PCBs Phenol	Benzene Carbon Tetrachloride Chlorobenzene Chloroform 1,1-Dichloroethane 1,1-Dichloroethylene 1,2-Dichloroethane 1,2-Dichloroethylene Ethylbenzene Ethylene Dibromide Methylene Chloride MEK MTBE 2-Methylnaphthalene Naphthalene Tetrachloroethylene Toluene 1,1,1-Trichloroethane Trichloroethylene Vinyl Chloride Xylenes

These multipliers are embedded in the formulae contained in the spreadsheet.

8.10 HOME GROWN FRUITS AND VEGETABLES

Reminder: The consumption of homegrown fruits and vegetables is evaluated in version 1.6a of the *Residential ShortForm*. This pathway is not considered in version 1.6b.

8.10.1 NARRATIVE DESCRIPTION

The *Food Chain Exposure Assessment* was developed to support the *Residential ShortForm*, although its use can be generalized to the analysis of any situation where the consumption of fruit and vegetables grown in contaminated soil may be of concern. This analysis evaluates typical exposures to a gardener who ingests home grown produce. It does this in two parts: (1) estimating the contaminant concentration in the produce as a function of the contaminant's soil concentration, and (2) estimating the amount of home grown produce a typical receptor consumes.

This exposure pathway model is under review, and future versions of the *ShortForm* may incorporate a new or modified model.

The evaluation of the food chain exposure pathway, while commonly overlooked in disposal site risk characterizations, is potentially significant. The National Gardening Association (as reported in US EPA, 1989b) estimates that approximately 1.9 million households in New England (37%) maintain vegetable gardens, and that, nationwide, vegetable gardens are just slightly less common in urban households (26%) than in suburbia (33%).

8.10.1.1 Contaminants of Concern

The *Residential ShortForm* contains 49 chemicals commonly reported at M.G.L. c.21E disposal sites. These chemicals include metals, volatile organic compounds (VOCs) and semi-volatile organic compounds (SVOCs). Of these 49 compounds, the volatile organic compounds were *not* evaluated in the food chain assessment. It is believed that significant levels of these chemicals can not accumulate in a plant due to their volatile characteristic. In addition, *cyanide*, *phenol*, and *Bis(2-ethylhexyl)phthalate* were *not* evaluated in the food chain assessment due to insufficient evidence that these chemicals accumulate in plant tissue.

Table 8-17 lists the chemicals which were included in the food chain analysis. Note that the term PAHs includes seventeen of the forty-nine distinct *Residential ShortForm* chemicals.

TABLE 8-17

FOOD CHAIN ANALYSIS CONTAMINANTS OF CONCERN
arsenic cadmium chromium lead mercury nickel silver thallium zinc PAHs PCBs

8.10.1.2 Food Intake

There is, perhaps, no exposure factor in risk assessment which is as difficult to characterize as the American diet. Food consumption varies by both composition and mass: *what you eat* and *how much of it you eat*. Factors which affect a person's food intake include age, sex, health status, place of residence, season, religion and philosophical beliefs.

For this food chain analysis a typical market basket of fresh garden fruits and vegetables was created following the three steps described below. This simplified approach does contain many uncertainties due both to insufficient data and wide variations in food intake.

The market basket is based on information gathered by the U.S. Department of Agriculture in the 1977-78 USDA Nationwide Food Consumption Survey (USDA, 1983) and on data used by the U.S. EPA for assessing the land application of municipal sludge (US EPA, 1989d). Nineteen garden fruits and vegetables (listed in the first column of Table 8-18) are included in the market-basket and the average daily consumption rates for the *homegrown* fruits or vegetables were calculated for different age groups as described below.

STEP 1: The relationship between the amount of homegrown produce and total ingested produce was described. This was done by subtracting the amount (lbs/week)

of produce purchased from the total amount of produce eaten (E). The difference (D) is assumed to be homegrown. The ratio D/E give the proportion of the total intake which is considered to be homegrown for this evaluation. This information is specific to households in the New England states (US DA, 1983). The population considered was made up of families in all types of urbanization (central city, suburban and non-metropolitan). The intakes were averaged over the entire year.

TABLE 8-18

PROPORTION OF FRESH PRODUCE THAT IS HOMEGROWN¹ ** for the General Population ** (Northeastern U.S.)				
PRODUCE	Amount Eaten (E) (lbs/wk)	Amount Bought (lbs/wk)	Difference (D) (lbs/wk)	Proportion D/E
White Potato	2.94	2.77	0.17	0.0578
Lettuce	1.27	1.22	0.05	0.0394
Spinach	0.08	0.07	0.01	0.1250
Cabbage	0.54	0.48	0.06	0.1111
Broccoli	0.23	0.22	0.01	0.0435
Cauliflower	0.09	0.08	0.01	0.1111
Peppers	0.26	0.22	0.04	0.1538
Beans (wax)	0.28	0.16	0.12	0.4286
Peas	0.04	0.02	0.02	0.5000
Beets	0.06	0.01	0.05	0.8333
Carrots	0.46	0.41	0.05	0.1087
Onions	0.60	0.55	0.05	0.0833
Corn	0.56	0.40	0.16	0.2857
Cucumbers	0.50	0.38	0.12	0.2400
Pumpkin, Squash	0.21	0.10	0.11	0.5238
Strawberries	0.11	0.09	0.02	0.1818
Tomatoes	1.14	0.66	0.48	0.4211
Cantaloupe	0.59	0.54	0.05	0.0847
Other Berries	0.06	0.03	0.03	0.5000
1 - Taken from US DA (1983), Tables 12, 13, and 14. The amount eaten (E) is based on the average family size of 3.06 members/household in this survey.				

STEP 2: The total produce intakes (purchased + homegrown) were identified (US EPA, 1989d) for four age groups: 0.5 to 1 year old, 2 years old, 14 to 16 years old, and 26 to 30 years old. These produce-specific intakes are given in dry weight, and are listed in Table 8-19.

TABLE 8-19

AVERAGE DAILY INTAKE OF PRODUCE

(Dry Weight)

**** General Population ****

Produce	Total Intake 0.5 < 1 yr g/day	Total Intake 2 year old g/day	Total Intake 14 < 16 yr (g/day)	Total Intake 26 < 30 yr (g/day)
White Potato (136, 137, 139, 143)	0.8390	2.4001	3.8646	4.2338
Lettuce (109, 147)	0.0053	0.1071	0.5466	0.9468
Spinach (107)	0.0160	0.0470	0.0470	0.2000
Cabbage (110, 111)	0.0143	0.0539	0.1900	0.2700
Broccoli (113)	0.0300	0.1100	0.1400	0.3600
Cauliflower (116)	0	0.0271	0.0283	0.0582
Peppers (125)	0.0005	0.0046	0.0200	0.0700
Beans (wax) (121)	0.0278	0.0724	0.0967	0.1878
Peas (046)	0.1700	0.1200	0.1600	0.3000
Beets (131)	0.0021	0.0371	0.0806	0.0976
Carrots (127, 143)	0.2016	0.3993	0.3340	0.6109
Onions (128, 139, 142, 148)	0.0206	0.0606	0.3391	0.3065
Corn (054)	0.1000	1.04	2.0900	1.5300
Cucumbers (123)	0.0070	0.0380	0.0870	0.1700
Pumpkin, Squash (126, 124)	0.1264	0.0590	0.1153	0.2773
Strawberries (086)	0.0500	0.1200	0.1600	0.1900
Tomatoes (117, 142, 151, 120)	0.0627	0.3462	0.6887	1.1263
Cantaloupe (089)	0.0561	0.0631	0.3010	0.2824
Other Berries (065)	0.0005	0.0082	0.0110	0.0114

Dry weight of food taken from U.S. EPA (1989d), Table A1-3. The numbers in parentheses by the food name refers to the lines in that Table which were used.

STEP 3: The average daily intake of homegrown produce was estimated for each fruit and vegetable by multiplying the proportion of homegrown to total (calculated in Table 8-18) by the total intake (Table 8-19) of each plant. The results are shown in Table 8-20.

TABLE 8-20

AVERAGE DAILY INTAKE OF Homegrown PRODUCE

(Dry Weight)

**** General Population ****

Produce	Homegrown Intake 0.5 < 1 yr g/day	Homegrown Intake 2 year old g/day	Homegrown Intake 14 < 16 yr (g/day)	Homegrown Intake 26 < 30 yr (g/day)
White Potato	0.0485	0.1387	0.2234	0.2447
Lettuce	0.0002	0.0042	0.0213	0.0369
Spinach	0.0020	0.0059	0.0059	0.0250
Cabbage	0.0016	0.0060	0.0211	0.0300
Broccoli	0.0013	0.0047	0.0060	0.0155
Cauliflower	0	0.0030	0.0031	0.0065
Peppers	0.0001	0.0007	0.0031	0.0108
Beans (wax)	0.0119	0.0311	0.0415	0.0806
Peas	0.0850	0.0600	0.0800	0.1500
Beets	0.0017	0.0309	0.0671	0.0813
Carrots	0.0220	0.0435	0.0364	0.0666
Onions	0.0017	0.0050	0.0281	0.0254
Corn	0.0286	1.2974	0.5977	0.4376
Cucumbers	0.0017	0.0091	0.0209	0.0408
Pumpkin, Squash	0.0662	0.0309	0.0604	0.1453
Strawberries	0.0091	0.0218	0.0291	0.0346
Tomatoes	0.0264	0.1458	0.2899	0.4742
Cantaloupe	0.0048	0.0054	0.0256	0.0240
Other Berries	0.0003	0.0041	0.0055	0.0057
<p>Dry weight of homegrown produce is the product of the proportion of produce eaten which is homegrown (D/E) and the Total Intake (TI) of produce for each age group. These factors are shown in Tables 8-18 and 8-19, respectively.</p> <p>D/E * TI = Homegrown Intake</p>				

The use of this hypothetical market basket indicates that the "average" adult receptor (25 to 30 years of age) ingests approximately 11.2 grams (≈ 0.4 ounces, dry weight) of fresh vegetables and garden fruits per day and that approximately 17% of that total is home grown. (0.4 ounces, dry weight is approximately equal to 4 ounces wet weight.) In this analysis, "fresh" includes all the fresh produce used by the families surveyed in the US Department of Agriculture study, including that eaten fresh, cooked or preserved for later use.

Note that the produce consumption information is available for four age periods which do not correspond with the receptors of interest to this evaluation. Some modification of these values is thus necessary, and the resulting intake values are presented in Table 8-21.

SUBCHRONIC EXPOSURES: The homegrown garden produce intake of the 1 to 2 year old child who is the receptor of concern for the *ShortForm* evaluation of subchronic exposures is assumed to be equal to the Total Intake of the 2 year old given in Table 8-20 (column 3). The assumed daily intake rates of homegrown fruits and vegetables are listed in Table 8-21 for the 1 to 2 year old receptor.

CHRONIC EXPOSURES: The receptor of concern for the *ShortForm* evaluation of chronic exposures is a child 1 to 8 years old, a period of seven years. The intakes for the 2 year old (Table 8-20, column 3) is assumed to be equal to the intakes for the first 4 years of the chronic exposure (ages 1 - 5 years) and the intake of the 14 to 16 year old (Table 8-20, column 4) is assumed to be equal to the intakes for the last 3 years of the chronic exposure (ages 5 - 8 years). Thus the homegrown produce intake used in the estimates for chronic exposure are weighted averages of the values presented in Table 8-19:

$$\text{Intake}_{1-8 \text{ yr}} = [(4 * \text{Intake}_{2 \text{ yr}}) + (3 * \text{Intake}_{14-16 \text{ yrs}})] \div 7$$

The resulting intake rates of homegrown fruits and vegetables are listed in Table 8-21 for the 1 to 8 year old receptor.

30 YEAR EXPOSURE: The receptor of concern for the cancer risk evaluations in the *ShortForm* is exposed for 30 years from birth to age 30. As with the chronic exposure detailed above, the intake of homegrown fruits and vegetables used for this pathway evaluation is a weighted average of the four time periods for which consumption information is available (Table 8-19).

$$\text{Intake}_{0-30 \text{ yrs}} = [(\text{Intake}_{<1}) + (4 * \text{Intake}_{2 \text{ yr}}) + (13 * \text{Intake}_{14-16 \text{ yr}}) + (12 * \text{Intake}_{26-30 \text{ yr}})] \div 30$$

The resulting intake rates of homegrown fruits and vegetables are listed in Table 8-21 for the 0 to 30 year old receptor.

TABLE 8-21

AVERAGE DAILY INTAKE OF <u>HOMEGROWN</u> PRODUCE (Dry Weight) ** General Population **			
Produce	Homegrown Intake 1 < 2 yrs ¹ g/day	Homegrown Intake 1 < 8 yrs ² g/day	Homegrown Intake 0 < 30 yrs ³ g/day
White Potato	0.139	0.175	0.215
Lettuce	0.004	0.012	0.025
Spinach	0.006	0.006	0.013
Cabbage	0.006	0.012	0.022
Broccoli	0.005	0.005	0.01
Cauliflower	0.003	0.003	0.004
Peppers	0.001	0.002	0.006
Beans (wax)	0.031	0.035	0.055
Peas	0.060	0.069	0.106
Beets	0.031	0.046	0.066
Carrots	0.043	0.04	0.049
Onions	0.005	0.015	0.023
Corn	0.297	0.426	0.474
Cucumbers	0.009	0.014	0.027
Pumpkin, Squash	0.031	0.044	0.091
Strawberries	0.022	0.025	0.03
Tomatoes	0.146	0.208	0.336
Cantaloupe	0.005	0.014	0.021
Other Berries	0.004	0.005	0.005
1 - The 1 < 2 year old is assumed to have the same intake of homegrown fruits and vegetables as the 2 year old in Table 8-20. 2 - The average daily 1 < 8 year old intake rate is a weighted combination of the intake rates of the 2 year old (weight = 4) and the 14<16 year old (weight = 3) in Table 8-20: $\text{Intake}_{1-8} = [(4 * \text{Intake}_2) + (3 * \text{Intake}_{14<16})] \div 7$ 3 - The average daily 0 < 30 year old intake is a weighted combination of the four age groups for which intakes are presented in Table 8-20: $\text{Intake}_{0-30} = [(\text{Intake}_{<1}) + (4 * \text{Intake}_2) + (13 * \text{Intake}_{14<16}) + (12 * \text{Intake}_{26<30})] \div 30$			

8.10.1.3 Plant Uptake

As described by Chaney (1984), plant absorption of chemicals from soil is related to: (1) chemical properties; (2) soil properties (pH, chemical concentration in the soil, organic matter, cation exchange capacity, and the level of other chemicals in the soil), and (3) plant properties (plant age, species, and the type of edible portion of the crop [leafy or root vegetable, or garden fruit]). This food chain analysis simplifies the complicated issues surrounding the plant uptake coefficients by focussing on chemical concentration in soil and the species of plant.

The accumulation of different chemicals has been reviewed extensively in studies of potential effects of sewage sludge application on cropland. Many of the uptake factors used in this analysis were found in such reviews. Table 8-22 lists the plant uptake factors used in this evaluation and gives the references for the specific values.

8.10.1.4 Output

The *Food Chain Exposure Assessment* does *not* calculate risk estimates directly, unlike the other exposure pathways in the *ShortForm*. For each chemical, three distinct risk Multipliers are derived through this analysis and these are used in conjunction with chemical specific factors (such as soil concentration and toxicity) in the *Residential ShortForm* to estimate risk. The Multipliers are listed in Table 8-23, and are contained in the TOXICITY INFORMATION section of the *ShortForm*.

These multipliers incorporate plant uptake factors, produce-specific intake rates, home grown fraction, bodyweight and units conversion factors. The multiplier is a fruit and vegetables pathway exposure factor, similar to that described by McKone (1989), which represents vegetable contaminant intake normalized to body weight and expressed in soil equivalents. The numerical value of the multiplier represents the mass of soil which contains the mass of contaminant in the daily homegrown intake of all of the fruits or vegetables, divided by the body weight of the receptor.

There are three multipliers for each chemical evaluated in this pathway, the Subchronic Hazard Index Multiplier, the Chronic Hazard Index Multiplier and the Cancer Risk Multiplier.

Each Multiplier is specific to a chemical, type of exposure and age group (chronic, subchronic) and health endpoint (threshold, carcinogenic). All Multipliers are expressed in units of $\text{Kg}_{\text{soil}}/(\text{Kg}_{\text{bw}} * \text{day})$, which is sometimes simplified to 1/day. The specific equations which use these Multipliers in risk characterization are

described in more detail in Section 9.0. The three *risk multipliers* derived for each chemical evaluated are:

The **Subchronic Hazard Index Multiplier, SHIM**, is used in the evaluation of the potential risks of *threshold* (i.e., noncarcinogenic) health effects following a short term exposure. The receptor of concern is the 1-2 year old infant who ingests approximately 0.03 ounces (dry weight) of home grown fruits and vegetables per day.

The **Chronic Hazard Index Multiplier, CHIM**, is used in the evaluation of the potential risks of *threshold* (i.e., noncarcinogenic) health effects following an extended exposure (seven years or more). The receptor of concern is the 1-8 year old child who ingests approximately 0.04 ounces (dry weight) of home grown fruits and vegetables per day.

The **Cancer Risk Multiplier, CRM**, is used in the estimation of a receptor's *Excess Lifetime Cancer Risk* resulting from an exposure of any specified duration. The receptor of concern in this evaluation experiences an exposure of a typical residential duration (30 years), eating approximately 0.05 ounces (dry weight) of home grown fruits and vegetables per day.

TABLE 8-22

PLANT UPTAKE FACTORS

$$K_{sp_{\text{plant/soil}}} = (mg_{\text{O+M}}/Kg_{\text{plant}})/(mg_{\text{O+M}}/Kg_{\text{soil}})$$

(References)

Produce	ARSENIC	CADMIUM	CHROMIUM	LEAD	MERCURY	NICKEL
White Potato	0.0006	0.03	0.11 (1)	0.0008	0.0033	0.125
Lettuce	0.04	0.43	0.0075 (2)	0.008	0.007	0.09
Spinach	0.04	0.43	0.0075 (3)	0.008	0.007	0.09
Cabbage	0.04	0.43	0.0075 (2)	0.008	0.007	0.09
Broccoli	0.04	0.43	0.0075 (2)	0.008	0.007	0.09
Cauliflower	0.04	0.43	0.0075 (2)	0.008	0.007	0.09
Peppers	0.002	0.05	0.01 (2,4)	0.002	0.0033	0.04
Beans (wax)	0.0002	0.01	0.81 (1)	0.001	0.001	0.13
Peas	0.0002	0.01	0.81 (1)	0.001	0.001	0.13
Beets	0.02	0.22	0.0125 (5)	0.003	0.017	0.52
Carrots	0.02	0.22	0.0125 (5)	0.003	0.017	0.52
Onions	0.02	0.22	0.0125 (5)	0.003	0.017	0.52
Corn	0.0001	0.03	0.0125 (5)	0.01	0.0033	0.13
Cucumbers	0.002	0.05	0.0125 (5)	0.002	0.0033	0.04
Pumpkin, Squash	0.002	0.05	0.0125 (5)	0.002	0.0033	0.04
Strawberries	0.002	0.05	0.0125 (5)	0.002	0.0033	0.04
Tomatoes	0.002	0.05	0.0125 (5)	0.002	0.0033	0.04
Cantaloupe	0.002	0.05	0.0125 (5)	0.002	0.0033	0.04
Other Berries	0.002	0.05	0.0125 (5)	0.002	0.0033	0.04

All uptake factors taken from U.S. EPA (1989d) unless otherwise noted:

- (1) - Grant, 1977
- (2) - Baes, 1984
- (3) - Walsh, 1977
- (4) - Cary, 1990
- (5) - Rinne, 1986

continued...

TABLE 8-22, *continued...*

PLANT UPTAKE FACTORS, <i>continued...</i>					
(References)					
Produce	SILVER	THALLIUM	ZINC	PAHs	PCBs
White Potato	0.8 (5)	0.0004 (2)	0.02	0.42	0.02
Lettuce	0.8 (5)	0.0004 (2)	0.8	0.29	0.38
Spinach	0.8 (5)	0.0004 (2)	0.8	0.29	0.38
Cabbage	0.8 (5)	0.0004 (2)	0.8	0.29	0.38
Broccoli	0.8 (5)	0.0004 (2)	0.8	0.29	0.38
Cauliflower	0.8 (5)	0.0004 (2)	0.8	0.29	0.38
Peppers	0.8 (5)	0.0004 (2)	0.04	0.42	0.02
Beans (wax)	0.8 (5)	0.0004 (2)	0.04	0.42	0.002
Peas	0.8 (5)	0.0004 (2)	0.04	0.42	0.002
Beets	0.8 (5)	0.0004 (2)	0.05	0.61	0.36
Carrots	0.8 (5)	0.0004 (2)	0.05	0.61	0.36
Onions	0.8 (5)	0.0004 (2)	0.05	0.61	0.36
Corn	0.8 (5)	0.0004 (2)	0.04	0.42	0
Cucumbers	0.8 (5)	0.0004 (2)	0.04	0.42	0.02
Pumpkin, Squash	0.8 (5)	0.0004 (2)	0.04	0.42	0.02
Strawberries	0.8 (5)	0.0004 (2)	0.04	0.42	0.02
Tomatoes	0.8 (5)	0.0004 (2)	0.04	0.42	0.02
Cantaloupe	0.8 (5)	0.0004 (2)	0.04	0.42	0.02
Other Berries	0.8 (5)	0.0004 (2)	0.04	0.42	0.02
All uptake factors taken from U.S. EPA (1989d) <u>unless</u> otherwise noted:					
(2) -	Baes, 1984				
(5) -	Rinne, 1986				

8.10.2 Equations

The general equation (modified from McKone, 1989) used to calculate the Multipliers for a given chemical (i) is given as:

$$M_i = \sum_j [HGFI_j * Ksp_{ij} * D2 * C \div BW \div AP] \quad (7)$$

Where:

M_i	=	The <u>M</u> ultiplier for chemical (i): Either the <u>C</u> ancer <u>R</u> isk <u>M</u> ultiplier (CRM), the <u>C</u> hronic <u>H</u> azard <u>I</u> ndex <u>M</u> ultiplier (CHIM), or the <u>S</u> ubchronic <u>H</u> azard <u>I</u> ndex <u>M</u> ultiplier (SHIM). In units: $Kg_{soil} / (Kg_{bw} * day)$									
$HGFI_j$	=	The <u>H</u> ome <u>G</u> rown <u>F</u> ood <u>I</u> ntake (dry weight) of the fresh produce (j) consumed (Table 8-21). In units: grams/day									
Ksp_{ij}	=	The steady state partition coefficient (Uptake Factor) for chemical (i) between the dry mass of vegetable (j) and the soil (Table 8-22). In units: $(mg/Kg_j) / (mg/Kg_{soil})$									
$D2 \& AP$	=	The <u>D</u> uration of the exposure period and the <u>A</u> veraging <u>P</u> eriod. For the purposes of these evaluations, the food chain exposures are assumed to occur over the relevant age of the receptor: <table> <tr> <td>Subchronic:</td><td>D2 = 1 year</td><td>AP = 1 year</td></tr> <tr> <td>Chronic:</td><td>D2 = 7 years</td><td>AP = 7 years</td></tr> <tr> <td>Lifetime:</td><td>D2 = 30 years</td><td>AP = 75 years</td></tr> </table>	Subchronic:	D2 = 1 year	AP = 1 year	Chronic:	D2 = 7 years	AP = 7 years	Lifetime:	D2 = 30 years	AP = 75 years
Subchronic:	D2 = 1 year	AP = 1 year									
Chronic:	D2 = 7 years	AP = 7 years									
Lifetime:	D2 = 30 years	AP = 75 years									
BW	=	The receptor's average <u>B</u> ody <u>W</u> eight over the exposure period. In units: Kg_{bw}									
C	=	<u>C</u> onversion factor: $10^{-3} Kg/g_i$									

The type of Multiplier derived (SHIM, CHIM, or CRM) is determined by the exposure scenario chosen and the corresponding input values. The Multipliers used in the *Residential ShortForm* are given in Table 8-23.

The equation used to evaluate potential *non-carcinogenic* effects associated with the consumption of homegrown fruits and vegetables is given as:

$$HI = \frac{HIM * [OHM]_{soil} * RAF}{RfD} \quad (8)$$

The equation used to evaluate potential *carcinogenic* effects associated with the consumption of homegrown fruits and vegetables is given as:

$$\text{ELCR} = \text{CRM} * [\text{OHM}]_{\text{soil}} * \text{RAF} * \text{CPV} \quad (9)$$

Where the exposure related terms (not shaded above) are:

- HIM = The Hazard Index Multiplier for the chemical: Either the Chronic Hazard Index Multiplier (CHIM, in the TOXICITY INFORMATION section of the ShortForm), or the Subchronic Hazard Index Multiplier (SHIM, in the TOXICITY INFORMATION section of the ShortForm). In units: $\text{Kg}_{\text{soil}} / (\text{Kg}_{\text{bw}} * \text{day})$
- CRM = The Cancer Risk Multiplier (CRM, in the TOXICITY INFORMATION section of the ShortForm). In units: $\text{Kg}_{\text{soil}} / (\text{Kg}_{\text{bw}} * \text{day})$
- $[\text{OHM}]_{\text{soil}}$ = The Operational Exposure Point Concentration (EPC) of the oil or hazardous material in the soil.
- RAF = The Relative Absorption Factor for food intake. RAFs are specific to the chemical, route of exposure and toxicity information. RAFs are presented for the evaluation of *non-carcinogenic* effects and for *carcinogenic* effects. Appendix C. Dimensionless.

TABLE 8-23

FOOD CHAIN MULTIPLIERS			
(from the <i>Residential ShortForm</i>)			
Oil or Hazardous Material	CANCER RISK MULTIPLIER 1/day	SUBCHRONIC HAZARD INDEX MULTIPLIER 1/day	CHRONIC HAZARD INDEX MULTIPLIER 1/day
ARSENIC	7.1E-08	3.0E-07	2.6E-07
CADMIIUM	NC	5.0E-06	4.4E-06
CHROMIUM	NC	9.2E-06	6.8E-06
LEAD	NC	3.8E-07	3.4E-07
MERCURY	NC	5.0E-07	4.5E-07
NICKEL	NC	1.1E-05	9.5E-06
SILVER	NC	6.5E-05	5.5E-05
THALLIUM	NC	3.2E-08	2.8E-08
ZINC	NC	4.8E-06	4.3E-06
PCBs	9.4E-07	4.3E-06	3.6E-06
CARCINOGENIC PAHs	6.9E-06	3.5E-05	3.0E-05
NON- CARCINOGENIC PAHs	NC	3.5E-05	3.0E-05
1/day is simplified from $K_{g_{soil}}/(K_{g_{BW}} * \text{day})$			
NC - Not Calculated (The chemical is assumed not to be carcinogenic via the oral route, <u>or</u> no carcinogenic potency value is available.			

TABLE 8-24

INGESTION OF FOOD - EXPOSURE ASSUMPTIONS			
Parameter	Subchronic Hazard Index Multiplier (SHIM)	Chronic Hazard Index Multiplier (CHIM)	Cancer Risk Multiplier (CRM)
Body Weight, BW	10.5 kg	16.8 kg	42.3 kg
Homegrown Food Intake, HGFI _i	0.85 g/day dry weight (0.03 oz/d)	1.16 g/day dry weight (0.04 oz/d)	1.6 g/day dry weight (0.06 oz/d)
Plant Uptake Coefficient, Ksp _u	0.0001 - 0.81	0.0001 - 0.81	0.0001 - 0.81
Relative Absorption Factor, RAF	0.006 -> 1.3	0.006 -> 1.3	0.006 -> 1.3

8.11 VAPORS - INDOOR AIR

8.11.1 NARRATIVE DESCRIPTION

The *Residential ShortForm* includes an evaluation of exposures which may result from the presence of chemicals in indoor air. Of particular concern are those groundwater contaminants which may volatilize and infiltrate a residence, although any situation in which the indoor air is impacted by oil or hazardous material from a disposal site must be evaluated. Only those chemicals considered to be volatile are included in the indoor air pathway, and these chemicals are listed in Table 8-25.

TABLE 8-25

CHEMICALS INCLUDED IN THE INDOOR AIR EXPOSURE PATHWAY	
Benzene	Carbon Tetrachloride
Chlorobenzene	Chloroform
1,1-Dichloroethane	1,2-Dichloroethane
1,2-Dichloroethylene	Ethylbenzene
Ethylene Dibromide	Mercury
Methylene Chloride	Methyl Ethyl Ketone
Methyl t-Butyl Ether	Phenol
Tetrachloroethylene	Toluene
1,1,1-Trichloroethane	Trichloroethylene
Vinyl Chloride	Xylenes

In the evaluation of **subchronic exposures**, the 1-2 year old receptor is assumed to be continuously exposed (24 hours/day) for a period of one month. (Exposures of duration less than one month would be considered *acute*, and are not evaluated in the *Residential ShortForm*.)

For **chronic exposures** and **lifetime exposures**, receptors are assumed to spend an average of 16 hours per day in the home.

8.11.2 EQUATIONS

The equation used to evaluate potential *non-carcinogenic* effects associated with inhalation of contaminated indoor air is given as:

$$HI = \frac{[OHM]_{air} * F * D1 * D2}{RfC_{inh} * AP} \quad (10)$$

The equation used to evaluate potential *carcinogenic* effects associated with inhalation of contaminated indoor air is given as:

$$ELCR = \frac{[OHM]_{air} * F * D1 * D2 * UR_{inh}}{AP} \quad (11)$$

Where the exposure related terms (not shaded above) are:

$[OHM]_{air}$ = The Operational Exposure Point Concentration (EPC) of the oil or hazardous material in indoor air. In units: $\mu\text{g}/\text{m}^3$.

F & D1 = The Frequency (F) of exposure and the Duration (D1) of each exposure event. The receptors are assumed to be continuously exposed to the contaminated indoor air while they are in the home. For subchronic exposure:

$$F = 1 \text{ event}/24 \text{ hr and } D1 = 24 \text{ hr/event}$$

The product of these terms is equal to 1, and it is dimensionless. They have thus been eliminated from the actual formulae contained in the spreadsheet.

For chronic and lifetime exposures:

$$F = 1 \text{ event}/24 \text{ hr and } D1 = 16 \text{ hr/event}$$

D2 and AP = The Duration (D2) of the exposure period and the Averaging Period (AP). For the purposes of these evaluations, the indoor air exposures are assumed be of durations:

Subchronic:	D2 = 1 month	AP = 1 month
Chronic:	D2 = 7 years	AP = 7 years
Lifetime:	D2 = 30 years	AP = 75 years

3. SUMMARY OF INDOOR AIR EXPOSURE PARAMETERS

TABLE 8-26

INHALATION OF INDOOR AIR - EXPOSURE ASSUMPTIONS			
Parameter	for Subchronic HI Calculations	for Chronic HI Calculations	for ELCR Calculations
Frequency of Exposure, F	1 event/24 hr	1 event/24 hr	1 event/24 hr
Duration of Exposure Event, D1	24 hr/event	16 hr/event	16 hr/event
Duration of Exposure Period, D2	1 month	7 years	30 years
Averaging Period, AP	1 month	7 years	75 years

8.11.4 EXPOSURE PARAMETERS

The methodology for evaluating indoor air differs from that used for other exposure pathways in that *Reference Concentrations* and *Unit Risks* are used in lieu of Reference Doses and Carcinogenic Potency Values. Since concentration and not dose is the basis of these toxicity values, body weight, respiration rate and RAFs are not incorporated in the formulae.

In general, the exposure period (D2) may be thought of as the span of the receptor's lifetime during which the exposures occur at some intermittent rate. How often the receptor is exposed during that time is the Frequency (F) and the duration of each individual exposure event is D1.

By definition, the Excess Lifetime Cancer Risk is estimated from a lifetime average daily exposure, and the averaging period for these calculations is the length of a

lifetime (75 years) no matter how long the exposure duration may be. In other words, even if a receptor were exposed a single time ($D2 = 1$ day), the exposure would be averaged over a lifetime ($AP = 75 \text{ years} * 365 \text{ days/year}$). In the calculation of a Hazard Index, however, the exposure of interest is that which the receptor experiences *during* the exposure period, and so the averaging period is set equal to that exposure period ($AP = D2$).

8.11.4.1 Frequency of Exposure, F

For each of the exposures evaluated (subchronic, chronic and lifetime), the receptor is assumed to be exposed to the volatilized OHM in the indoor air of the home each and every day. Thus each day is considered to include an exposure "event", and this is mathematically represented as "1 event/24 hours".

8.11.4.2 Duration of the Exposure Event, D1

While all the receptors are considered to be exposed each and every day, the evaluation assumes that the older receptors do not spend all of their time indoors. The time spent out of the home (in school, at play or at work) is reflected in the duration of the exposure event. On average these receptors are assumed to spend 8 hours/day away from home, and $D1$ is thus $24 - 8 = 16$ hours/event. The receptor for the subchronic exposure (the 1-2 year old child) is assumed to remain in the home virtually 24 hours/day during the exposure period.

8.11.4.3 Duration of the Exposure Period, D2

For a residential indoor air exposure, the exposure period depends on how long the receptor lives in the affected house. The *Residential ShortForm* assumes that the receptor may live in the same house for up to 30 years, representing the 95th percentile of a typical duration of residence (U.S. EPA, 1989b), and thus $D2$ is contingent on the definitions of subchronic, chronic and residency exposures. Since a subchronic exposure may range from 1 month to 7 years, $D2_{\text{subchronic}} = 1$ month; chronic exposure may range from seven years to a lifetime, and $D2_{\text{chronic}} = 7$ years; for the cancer risk calculations, the duration of the exposure period is equal to the expected residence time in the affected home, and $D2_{\text{cancer}} = 30$ years.

8.11.4.4 Averaging Period, AP

For subchronic and chronic Hazard Index calculations, the averaging period is equal to the duration of exposure ($D2$). For the evaluation of Excess Lifetime Cancer Risk, the Averaging Period is equal to 75 years.

9.0 RISK CHARACTERIZATION

9.1 Purpose

The purpose of the MCP Phase II Health Risk Characterization is to provide the necessary information which will allow a site manager to answer the question, "*Based upon the risk of harm to public health, is remediation necessary at this disposal site?*". (See Section 10.0 - Conclusions.)

As described in Section 4.2, the Massachusetts Contingency Plan details very specific risk management criteria to be used in the determination of the need for remediation. These criteria include public health standards and the Total Site Risk Limits contained in 310 CMR 40.545(3)(g)3b. These criteria are also employed in the evaluation of remedial alternatives which is part of the MCP Phase III.

The Risk Characterization portion of the risk assessment combines the results of the Hazard Identification, Dose-Response Assessment and the Exposure Assessment to yield quantitative measures of risk (the Hazard Index and Excess Lifetime Cancer Risk) for each chemical in each exposure medium. These chemical-specific values are then combined to yield Total Site Cancer and Noncancer Risk estimates for the residential receptor who is the focus of *Residential ShortForm*. In addition, the Risk Characterization compares the calculated Exposure Point Concentrations to the applicable or suitably analogous public health standards identified for each exposure medium.

In order for the comparison to the MCP risk management criteria to be valid, it is important that the Exposure Point Concentrations (EPCs) and Total Site Risks be calculated in a manner consistent with Departmental guidance. Deviations from acceptable risk assessment methodology may result in the development of Exposure Point Concentrations and Total Site Risks which are not comparable to the risk management criteria and which could not be used to determine the need for remediation.

9.2 Comparison of EPC To Standards

The Massachusetts Contingency Plan requires that the characterization of risk of harm to human health include a comparison of current and reasonably foreseeable exposure point concentrations to applicable or suitably analogous public health standards (310 CMR 40.545(3)(g)).

9.2.1 Soil Standards

There are currently no applicable or suitably analogous public health standards for soil.

9.2.2 Drinking Water Standards

The *Risk Assessment ShortForm - Residential Scenario* automatically compares the site-specific Drinking Water Exposure Point Concentrations (typed into the DATA ENTRY section of the ShortForm by the risk assessor) to the Massachusetts Maximum Contaminant Levels (MMCLs).

The Massachusetts MCLs are contained in regulations promulgated by the Massachusetts Department of Environmental Protection, Division of Water Supply. These regulations are frequently updated, and revised copies of the Massachusetts Drinking Water Regulations (310 CMR 22.00) are available at the State Bookstore in Boston at (617) 727-8234 or Springfield (413) 784-1376. The *Residential ShortForm* will be updated annually to insure that the comparison to drinking water standards remains current.

The Massachusetts Drinking Water Standards are listed in the COMPARISON TO DRINKING WATER STANDARDS SUMMARY TABLE. The standards are given in units of $\mu\text{g}/\text{liter}$, and thus are directly comparable to the Exposure Point Concentrations entered by the user.

If the Exposure Point Concentration entered in the DATA ENTRY section of the *ShortForm* is **greater than** the listed drinking water standard for that chemical, a "1" is placed in the columns headed "EXCEEDS DW STD" (of the COMPARISON OF EPC TO DRINKING WATER STANDARDS SUMMARY TABLE). The *number* of exceedances summed and the total given at the bottom of the COMPARISON TO DRINKING WATER STANDARDS SUMMARY TABLE.

9.2.3 Fruit And Vegetables Standards

There are currently no applicable or suitably analogous public health standards for contaminants in food.

9.2.4 Vapors - Indoor Air

There are currently six (6) ambient air quality standards which are considered applicable or suitable analogous under the Massachusetts Contingency Plan. The Massachusetts Ambient Air Quality Standards (310 CMR 6.00) contain numerical criteria for sulfur oxides, PM₁₀, Carbon Monoxide, Ozone, Nitrogen Dioxide and Lead.

The indoor air exposure pathway developed for the *Residential ShortForm* (described in Section 8.4 and 8.5) is concerned with the infiltration of volatile organic compounds (VOCs) into a building from contaminated groundwater. There are no air standards for any of the VOCs of concern in this scenario, and thus no comparison of Exposure Point Concentration to standards can be made.

For sites where there is evidence of indoor air contamination not consistent with the infiltration model used in this spreadsheet, the *Residential ShortForm* may not provide a complete characterization of the potential human health risks.

9.3 Hazard Index

9.3.1 Narrative Description

The potential for *non-carcinogenic* (or *threshold*) health effects is characterized in the *Residential ShortForm* by the use of the **Hazard Index**.

For a given chemical, the Hazard Index is the ratio of a receptor's quantified exposure and the "acceptable" (or "allowable") exposure level. A Hazard Index of 1.0 would indicate that the receptor's exposure is equal to the "acceptable" exposure level, and it is considered unlikely that adverse health effects would occur. A Hazard Index greater than 1 does not imply that health impacts would necessarily be expected: the interpretation of the Hazard Index must consider the appropriateness of the exposure assumptions and the basis of the toxicity values used in the calculations. For the *Residential ShortForm*, the toxicity values are described in Section 7.0 - Dose Response Assessment, and the exposure assumptions for each receptor are described in Section 8.0 - Exposure Assessment.

In its most general form, the Hazard Index associated with a chemical via a route of exposure is calculated:

$$HI = ADD/RfD \quad (1)$$

or

$$HI = [OHM]_{air}/RfC \quad (2)$$

Where:

- HI = The Hazard Index associated with exposure to the chemical via the specified route of exposure. Dimensionless.
- ADD = The estimated Average Daily Dose of the chemical via the specified exposure route. In units: mg/kg/day.
- RfD = The oral Reference Dose or substitute toxicity value identified for the chemical of concern and appropriate to the specific exposure pathway. The selection of these toxicity values is described in Section 7.0. In units: mg/kg/day.
- [OHM]_{air} = The Exposure Point Concentration of the oil or hazardous material in air. In units: $\mu\text{g}/\text{m}^3$.
- RfC = The Reference Concentration or substitute toxicity value identified for the chemical of concern. The selection of the toxicity values is described in Section 7.0. In units: $\mu\text{g}/\text{m}^3$.

The Average Daily Dose in equation (1) above represents the "exposure related terms" which were described in Section 8.0. Factors such as the Exposure Point Concentration, Frequency of exposure and Body Weight are included in the ADD. Note that the *Residential ShortForm* does not calculate an average daily dose as a separate step: the actual equations contained in the spreadsheet combine the exposure and risk calculations.

Separate calculations are performed for the characterization of risk for the subchronic (1 year) and chronic (7 year) exposures for the residential receptors.

9.3.2 Equations

The following sections present the pathway-specific equations which are used to estimate the **Subchronic and Chronic Hazard Indices**. The actual equations contained in the *Residential ShortForm* combine the steps of calculating average daily dose and quantifying risk. The equations which follow are repeated from Section 8.0 and the portions of the equation specific to the quantification of dose are shaded here to highlight the risk related portion of each equation. [In Section 8.0, these risk terms were shaded.]

9.3.2.1 Soil

The equation (repeated from Section 8.7.2) used to evaluate potential non-carcinogenic effects associated with direct contact with contaminated surface soil is given as:

$$HI = \frac{[OHMI]_{soil} * ((NADSIR * RAF) + (NADSCR * RAF)) * C}{RfD} \quad (3)$$

where the risk-related terms (not shaded above) are:

HI = Either the Subchronic Hazard Index or the Chronic Hazard Index. These values represent the Hazard Index associated with exposure to the individual chemical through direct contact with the contaminated soils. Dimensionless.

RfD = The oral Reference Dose or substitute toxicity value identified for the particular chemical of concern. Either the Subchronic Oral RfD or the Chronic Oral RfD. In units of: mg/kg/day.

9.3.2.2 Drinking Water

The equation (repeated from Section 8.9.2) used to evaluate potential non-carcinogenic effects associated with exposure to contaminated drinking water is given as:

$$HI = \frac{[OHMI]_{dw} * VI * RAF * F * D1 * D2 * MULT}{RfD * BW * AP * C} \quad (4)$$

Where the risk-related (not shaded) portion of the equation is:

HI = Either the Subchronic Hazard Index or the Chronic Hazard Index. These values represent the Hazard Index associated with exposure to the individual chemical through the use of the contaminated drinking water. In units of: Dimensionless.

RfD = The oral Reference Dose or substitute toxicity value identified for the particular chemical of concern. Either the Subchronic Oral RfD or the Chronic Oral RfD. In units of: mg/kg/day.

9.3.2.3 Fruits and Vegetables

Reminder: The consumption of homegrown fruits and vegetables is evaluated in version 1.6a of the *Residential ShortForm*. This pathway is not considered in version 1.6b.

The equation (repeated from Section 8.10.2) used to evaluate potential *non-carcinogenic* effects associated with exposure to homegrown fruits and vegetables is given as:

$$HI = \frac{HIIM * [OHMI]_{soil} * RAF}{RfD} \quad (5)$$

Where the risk-related (not shaded) portion of the equation is:

- HI = Either the Subchronic Hazard Index or the Chronic Hazard Index. These values represent the Hazard Index associated with exposure to the individual chemical through the consumption of garden fruits and vegetables grown in the contaminated soil. In units of: Dimensionless.
- RfD = The oral Reference Dose or substitute toxicity value identified for the particular chemical of concern. Either the Subchronic Oral RfD or the Chronic Oral RfD. In units of: mg/kg/day.

9.3.2.4 Vapors - Indoor Air

The equation (repeated from Section 8.11.2) used to evaluate potential *non-carcinogenic* effects associated with exposure to vapors in indoor air is given as:

$$HI = \frac{[OHMI]_{air} * F * D1 * D2}{RfC * AP} \quad (6)$$

Where the risk-related (not shaded) portion of the equation is:

- HI = Either the Subchronic Hazard Index or the Chronic Hazard Index. These values represent the Hazard Index associated with exposure to the individual chemical through the inhalation of vapors in indoor air. In units of: Dimensionless.
- RfC = The Reference Concentration or substitute toxicity value identified for the particular chemical of concern. Either the Subchronic RfC or the Chronic RfC. In units of: $\mu\text{g}/\text{m}^3$.

9.4 Excess Lifetime Cancer Risk

9.4.1 Narrative Description

The potential for *carcinogenic* (i.e. non-threshold) health effects is characterized in the *Residential ShortForm* in the calculation of **Excess Lifetime Cancer Risk** (ELCR) for the residential receptor.

The *Residential ShortForm* calculates an excess lifetime cancer risk based upon a **30-year** exposure. The 30 year period was chosen as it represents the 95th percentile of the typical duration of residence in a house (US EPA, 1989b). The cancer risks associated with shorter exposure periods (i.e. the 1-year subchronic exposure or the 7-year chronic exposure) are not calculated. ELCR estimates for such exposures would be duplicative given the assumption of potential exposure during the entire 30 year residence time.

The 30-year exposure is *averaged* over a lifetime to yield the Lifetime Average Daily Dose necessary for the cancer risk calculations. Use of the Lifetime Average Daily Dose should not be interpreted to mean that the *ShortForm* assumed a lifetime exposure, however.

For a given chemical, the estimated ELCR is the product of the receptor's quantified exposure and a measure of carcinogenic potency. The resulting risk estimate is considered to be an upper-bound probability of the likelihood of developing cancer as a result of that exposure. As described in Section 7.12, the measures of carcinogenic potency employed in the *ShortForm* are the **Carcinogenic Potency Value (CPV)** and the **Unit Risk (UR)**. The assumptions used to quantify exposure are detailed in Section 8.0 - Exposure Assessment.

In its most general form, the Excess Lifetime Cancer Risk associated with exposure to a chemical via a particular pathway is estimated:

$$\text{ELCR} = \text{LADD} * \text{CPV} \quad (7)$$

or

$$\text{ELCR} = [\text{OHM}]_{\text{air}} * \text{UR} \quad (8)$$

Where:

ELCR =	The <u>Excess Lifetime Cancer Risk</u> associated with exposure to the chemical via the specified route of exposure. Dimensionless.
LADD =	The estimated <u>Lifetime Average Daily Dose</u> of the chemical via the specified exposure route. In units: mg/kg/day.
CPV =	The <u>Carcinogenic Potency Value</u> identified for the chemical of concern and appropriate to the specific exposure pathway. The identification and selection of the CPVs is described in Section 7.0. In units: (mg/kg/day) ⁻¹ .
[OHM] _{air} =	The Exposure Point Concentration of the <u>oil</u> or <u>hazardous material</u> in <u>air</u> . In units: µg/m ³ .
UR =	The <u>Unit Risk</u> for the particular chemical of concern. The identification and selection of the URs is described in Section 7.0. In units: µg/m ³ .

The Lifetime Average Daily Dose in equation (7) above represents the "exposure related terms" which were previously described in detail (Section 8.0). Factors such as the Exposure Point Concentration, Frequency of exposure and Body Weight are included in the LADD. Note that the *Residential ShortForm* does not calculate a lifetime average daily dose as a separate step: the actual equations contained in the spreadsheet combine the exposure and risk calculations.

9.4.2 Equations

The following subsections present the pathway-specific equations which are used to estimate the **Excess Lifetime Cancer Risks (ELCR)**. The actual equations contained in the *Residential ShortForm* combine the steps of quantifying exposure and estimating risk. The equations which follow are repeated from Section 8.0 and the portions of the equation specific to the quantification of exposure is shaded here to highlight the risk-related terms. [In Section 8.0, the risk portion of each equation was shaded.]

9.4.2.1 Soil

The equation (copied from Section 8.7.2) used to evaluate potential carcinogenic effects associated with direct contact exposure with contaminated surface soil is given as:

$$ELCR = [OHM]_{soil} * ((NLADSIR * RAF) + (NLADSCR * RAF)) * C * CPV_o \quad (9)$$

Where the risk-related terms (not shaded above) are:

CPVo = The oral Carcinogenic Potency Value for the particular chemical of concern. In units of: (mg/kg/day)⁻¹

ELCR = The Excess Lifetime Cancer Risk associated with exposure to the individual chemical through direct contact with the contaminated soils. Dimensionless.

9.4.2.2 Drinking Water

The equation (repeated from Section 8.9.2) used to evaluate potential *carcinogenic* effects associated with exposure to contaminated drinking water is given as:

$$ELCR = \frac{[OHM]_{dw} * VI * RAF * F * D1 * D2 * MULT * CPV_o}{BW * AP * C} \quad (10)$$

Where the risk-related terms (not shaded above) are:

CPVo = The oral Carcinogenic Potency Value for the particular chemical of concern. In units of: (mg/kg/day)⁻¹

ELCR = The Excess Lifetime Cancer Risk associated with exposure to the individual chemical through the use of the contaminated drinking water. Dimensionless.

9.4.2.3 Fruits and Vegetables

Reminder: The consumption of homegrown fruits and vegetables is evaluated in version 1.6a of the *Residential ShortForm*. This pathway is not considered in version 1.6b.

The equation (repeated from Section 8.10.2) used to evaluate potential *carcinogenic* effects associated with exposure to homegrown fruits and vegetables is given as:

$$\text{ELCR} = \text{CRM} * [\text{OHM}]_{\text{F}} * \text{RAF} * \text{CPV}_o \quad (11)$$

Where the risk-related terms (not shaded above) are:

ELCR = The Excess Lifetime Cancer Risk associated with exposure to the individual chemical through the consumption of homegrown fruits and vegetables. **Dimensionless.**

CPV_o = The oral Carcinogenic Potency Value for the particular chemical of concern. In units of: (mg/kg/day)

9.4.2.4 Vapors - Indoor Air

The equations used to evaluate potential *carcinogenic* effects associated with inhalation of vapors in indoor air is given as:

$$\text{ELCR} = \frac{[\text{OHM}]_{\text{I}} * \text{F} * \text{D1} * \text{D2} * \text{UR}_{\text{inh}}}{\text{AP}} \quad (12)$$

Where the risk-related terms (not shaded above) are:

ELCR = The Excess Lifetime Cancer Risk associated with exposure to the individual chemical through the inhalation of vapors present in indoor air. **Dimensionless.**

UR_{inh} = The inhalation Unit Risk for the particular chemical of concern.
In units of: (μg/m³)⁻¹

9.5 Total Site Risks

The *Residential ShortForm* estimates **Total Site Risks** for a residential receptor for both carcinogenic and noncarcinogenic health effects. These risks are then available to the site manager for decision making purposes under the MCP. Rather than simply providing a single, final "Total Risk" value, however, the *ShortForm* also details the chemical- and medium-specific risks which contribute to the Total Site Risks. The accessibility of these intermediate values provides additional information to the site manager which can be used in the development of remedial alternatives and target cleanup levels.

9.5.1 Noncarcinogenic Risk

The *Residential ShortForm* calculates several types of Hazard Indices for the evaluation of noncarcinogenic risk: **chemical-specific**, **route-specific**, and a **Total Hazard Index**.

$$HI_{\text{route-specific}} = \sum HI_{\text{chemical-specific}} \tag{13}$$

$$HI_{\text{Total}} = \sum HI_{\text{route-specific}} \tag{14}$$

The **chemical-specific hazard indices** (both subchronic and chronic) are presented in each of the exposure pathway SUMMARY TABLES respectively) of the *ShortForm*. These values are the hazard indices associated with each chemical for a given pathway. The chemical-specific HIs answer very pointed questions, such as: *"What is the non-carcinogenic risk associated with exposure to toluene in the indoor air?"*.

The **route-specific hazard indices** (both subchronic and chronic) are presented in each of the exposure pathway SUMMARY TABLES of the *ShortForm* (the Totals at the bottom of each table), and in the OVERALL HEALTH RISKS SUMMARY TABLE. These values represent the hazard indices associated with each exposure pathway. The route-specific HIs answer more general questions, such as: *"What is the non-carcinogenic risk associated with drinking the contaminated water at this site?"*

The **Total Hazard Indices** (both subchronic and chronic) are presented in the OVERALL HEALTH RISKS SUMMARY TABLE of the *ShortForm*. These values represent the hazard index associated with cumulative exposure experienced by the receptor. The Total Hazard Indices answer the most general question, *"What*

is the cumulative (non-carcinogenic) impact that this site might have on a residential receptor?" The Total Hazard Indices also answer the specific MCP question, "Is remediation required at this disposal site to eliminate a significant risk of harm to human health?"

The Total Hazard Index and the Route-Specific Hazard Indices calculated in the *Residential ShortForm* are actually screening Hazard Indices which sum the chemical-specific HIs of all the OHM in the relevant exposure pathways regardless of each chemical's health endpoint, mechanism of action or target organ.

Section 10.0 discusses the interpretation of the Hazard Index results within the context of the Massachusetts Contingency Plan and the use of these estimates as a risk management tool.

9.5.2 Carcinogenic Risk

The *Residential ShortForm* calculates several types of Excess Lifetime Cancer Risks: **chemical specific**, **route-specific**, and **Total Site Cancer Risk**.

$$ELCR_{\text{route-specific}} = \sum ELCR_{\text{chemical-specific}} \quad (15)$$

$$ELCR_{\text{Total}} = \sum ELCR_{\text{route-specific}} \quad (16)$$

The **chemical-specific** ELCRs are presented in each of the exposure pathway SUMMARY TABLES of the *ShortForm*. These values are the cancer risks associated with each chemical for a given pathway. The chemical-specific ELCRs answer very pointed questions, such as: *"What is the carcinogenic risk associated with exposure to benzene in the indoor air?"*.

The **route-specific** ELCRs are presented in each of the exposure pathway SUMMARY TABLES (the Totals at the bottom of each table), and in the OVERALL HEALTH RISKS SUMMARY TABLE. These values represent the excess lifetime cancer risks hazard associated with each exposure pathway. The route-specific ELCRs answer more general questions, such as: *"What is the carcinogenic risk associated with drinking the contaminated water at this site?"*

The **Total Site Cancer Risk** is presented in the OVERALL HEALTH RISKS SUMMARY TABLE of the *ShortForm*. This value represents the total excess lifetime cancer risk associated with the cumulative exposure experienced by the residential receptor. The Total Site Cancer Risk answers the most general

question, "*What is the cumulative (carcinogenic) impact that this site might have on a residential receptor?*" The Total Site Cancer Risk *also* answers the specific MCP question, "*Is remediation required at this disposal site to eliminate a significant risk of harm to human health?*"

The calculation of excess lifetime cancer risk is performed for those chemicals identified at the disposal site which are considered to be *known, probable* or *possible human carcinogens* (EPA Class A, B or C) and for which adequate toxicity information is available.

Section 10.0 discusses the interpretation of the Excess Lifetime Cancer Risk results within the context of the Massachusetts Contingency Plan and the use of this estimate as a risk management tool.

9.6 Results - SUMMARY TABLES

The *Residential ShortForm* contains six summary tables (five in version 1.6b) which present the results of the risk characterization for this residential exposure scenario. The printed summary tables provide the basis of the Phase II Risk Characterization Report required under the Massachusetts Contingency Plan, and should be submitted as part of any Report completed with the aid of the *ShortForm*.

9.6.1 Exposure Route Summary Tables

The four route-specific summary tables (#1-4: soils, drinking water, homegrown vegetables and indoor air) consist of six columns of information:

- the name of the Oil or Hazardous Material (OHM),
- the Exposure Point Concentration (EPC),
- the Operational Exposure Point Concentration (OEPC),
- the Subchronic Hazard Index (SHI),
- the Chronic Hazard Index (CHI), and
- the Excess Lifetime Cancer Risk (ELCR).

Reminder: Version 1.6b of the *Residential ShortForm* does not consider the homegrown fruits and vegetables pathway. Thus, version 1.6b has three route-specific summary tables.

► The names of the 49 Oil or Hazardous Material (OHM) included in the *ShortForm* are repeated at the left of each of these summary tables. This list is

identical to that contained in the DATA ENTRY section of the *ShortForm*, and will be updated as more chemicals are added to the spreadsheet.

- ▶ The Exposure Point Concentration (EPC, mg/kg) listed in the Summary Tables is the value entered by the risk assessor in the DATA ENTRY section of the *ShortForm*. If no value was entered for a given chemical this column will remain blank.
- ▶ The Operational Exposure Point Concentration (OEPC, mg/kg) listed in the Summary Tables is the value used within the spreadsheet to estimate the potential risks of harm to human health. The OEPC is determined by comparing the Exposure Point Concentration entered by the risk assessor to a standard "background" level contained in the TOXICITY INFORMATION section of the *ShortForm*.
 - If the EPC for a given OHM is less than the "background" level listed for that chemical, then the OEPC is set to zero and the OHM is not carried through quantitative the estimation of risk.
 - If the EPC for a given OHM is equal to or greater than the "background" level listed for that chemical, then the OEPC is set equal to the EPC and the chemical is carried through the quantitative risk characterization.

Note that the *Residential ShortForm* does not subtract out "background". This operation is included in the *ShortForm* in order to screen out of the quantitative risk assessment those chemicals present at levels consistent with "background". For a complete discussion of issues relating to the elimination of OHM from the quantitative risk assessment see Section 6.2.

- ▶ The Subchronic Hazard Index listed in the Summary Tables is the quantification of the potential *non-carcinogenic* risk of harm to health associated with a short-term (one year or less) residential exposure. The equations contained in this column are described in detail in Section 9.3. The chemical-specific results in the body of the Summary Table are summed at the bottom of the column to yield a route-specific Subchronic Hazard Index.
- ▶ The Chronic Hazard Index listed in the Summary Tables is the quantification of the potential *non-carcinogenic* risk of harm to health associated with a longer-term (one to seven years) residential exposure. The equations

contained in this column are described in detail in Section 9.3. The chemical-specific results in the body of the Summary Table are summed at the bottom of the column to yield a route-specific Chronic Hazard Index.

► The Excess Lifetime Cancer Risk (ELCR) listed in the Summary Tables is the quantification of the potential *carcinogenic* risk of harm to health associated with a 30-year residential exposure. The equations contained in this column are described in detail in Section 9.4. The chemical-specific results in the body of the Summary Table are summed at the bottom of the column to yield a route-specific Excess Lifetime Cancer Risk.

9.6.2 Comparison Of EPCs To Standards Summary Table

Summary Table 5 (Table 4 in version 1.6b) presents the comparison of Exposure Point Concentrations to Drinking Water Standards. This table consists of four columns:

- the name of the Oil or Hazardous Material (OHM),
- The Exposure Point Concentration (EPC),
- Any Drinking Water Standard for that chemical, and
- A notation if the EPC exceeds the standard.

► The first two columns are described above. The drinking water standards are taken from the applicable Massachusetts Drinking Water Regulations (310 CMR 22.00) as described in Section 9.2.

► The last column contains a notation (the character "1") if the exposure point concentration entered by the risk assessor exceeds the drinking water standard for that chemical. The number of exceedances is summed at the bottom of the column.

9.6.3 Overall Health Risk Summary

Summary Table 6 (table 5 in version 1.6b) presents a summary of the cumulative risks calculated for the residential exposure scenario. The table includes the route-specific risks estimated for direct contact with soil, for drinking water, for eating homegrown produce (excluded in version 1.6b) and for inhaling indoor air.

Total Site Risks are summarized at the bottom of the table for the Subchronic Hazard Index, Chronic Hazard Index and the Excess Lifetime Cancer Risk.

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10.0 CONCLUSIONS

As described previously (Sections 1.0 and 2.0), the *Residential ShortForm* has been developed primarily to streamline the baseline risk characterization process required as part of the Massachusetts Contingency Plan's Phase II investigation. The conclusions which may be drawn from the results of a *ShortForm* risk assessment are based on the risk management criteria (Section 4.0) which are contained in the MCP.

Alternative uses of this *ShortForm* beyond the c.21E/MCP universe may require the application of different sets of risk management criteria. It is important to identify *in advance* the decision-making criteria which would be employed in such cases, and to have the concurrence of the appropriate regulatory authority.

The MCP Phase II health risk characterization is designed to answer the question, "*Is remediation required at this disposal site?*". The health risk characterization is performed *after* the Comprehensive Site Assessment is completed: this insures that sufficient data has been collected to adequately characterize the extent of contamination and potential human exposures. Inadequate site information introduces an additional level of uncertainty which may undermine the conclusions of the risk characterization.

The conclusions of the *ShortForm* multi-media health risk characterization follow directly from the Massachusetts Contingency Plan.

The Department's Waste Site Cleanup is currently being redesigned in a manner which will result in significant changes in the Massachusetts Contingency Plan. As these changes are implemented, the *Residential ShortForm* and its *Documentation...* will be revised to reflect the new program.

10.1 When No Further Remedial Response Action Is Necessary

The risk assessor may conclude that no further remedial response action is necessary, *based on human health considerations*, if the disposal site will not pose a significant risk of harm to health during any foreseeable period of time. The risk assessor is referred to the specific regulations which concern this decision, contained in 310 CMR 40.545(3)(i).

The criteria used to conclude that no further action is necessary are:

- **The current and all reasonably foreseeable exposure point concentrations are less than or equal to any applicable or suitably analogous public health standards.** The *Residential ShortForm* automatically compares the groundwater exposure point concentrations entered by the risk assessor to the Massachusetts drinking water standards. Summary Table 5 (table 4 in version 1.6b) contains this comparison.
- **The current and reasonably foreseeable total site cancer risk is equal to or less than the total site cancer risk limit of one in one hundred thousand (1×10^{-5}) AND the total site non-cancer risk is equal to or less than the total site non-cancer risk limit which is a Hazard Index equal to 0.2.** The *Residential ShortForm* automatically calculates the total site cancer and non-cancer risks. These values are presented in Summary Table 4 - Overall Health Risk Summary (Table 3 in version 1.6b).

10.2 When A Remedial Response Action Is Necessary

Somewhat oddly, the Massachusetts Contingency Plan defines the need for remediation based upon the absence of significant risk, as described above. Remedial response actions are thus required when the site does not meet the conditions for No Further Remedial Response Action. 310 CMR 40.545(3)(j) provides the regulatory language for this determination. However it may be helpful to state, in english, the conditions when a remedial response action is required, *based upon human health considerations*.

A remedial response action is necessary, if:

- **The current and all reasonably foreseeable exposure point concentrations are greater than any applicable or suitably analogous public health standards.** The *Residential ShortForm* automatically compares the groundwater exposure point concentrations entered by the risk assessor to the Massachusetts drinking water standards. Summary Table 5 (Table 4 in version 1.6b) contains this comparison.
- **The current and reasonably foreseeable total site cancer risk is greater than the total site cancer risk limit of one in one hundred thousand (1×10^{-5}) OR the total site non-cancer risk is greater than the total site non-cancer risk limit which is a Hazard Index equal to 0.2.** The *Residential ShortForm* automatically calculates the total site cancer and non-cancer risks. These values are presented in Summary Table 4 - Overall Health Risk Summary (Table 3 in version 1.6b).

10.3 Phase II Health Risk Characterization Conclusion

The Phase II Report **must** contain conclusions based upon the characterization of risk of harm to human health (310 CMR 40.545(4)(j)).

The conclusions may be either that:

No Further Remedial Response Action is Necessary (based on human health considerations) if the human health risk characterization demonstrates that the disposal site meets the requirements set forth in 310 CMR 40.545(3)(i) and described above (Section 10.1), *or*

A Remedial Response Action Is Necessary (based on human health considerations) if the human health risk characterization demonstrates that a No Further Action (NFA) determination is not justified, as set forth in 310 CMR 40.545(3)(j) and described above (Section 10.1).

10.4 Safety, Public Welfare And The Environment

The *Residential ShortForm* addresses the characterization of risk of harm to human health. Use of the *ShortForm* does **NOT** absolve the risk assessor from the Massachusetts Contingency Plan requirement to characterize the risk of harm to safety, public welfare and the environment. The reader is referred to the MCP requirements set forth in 310 CMR 40.545(3)(h), 545(3)(i), 545(3)(j) and 545(4), which deal with the characterization of these risks and the determination of need for response actions.

Remediation may be required, based upon the risk of harm to safety, public welfare or the environment, *even if* no further remedial response action is necessary based upon human health considerations.

11.0 Uncertainty Analysis

11.1 Narrative Discussion

The key to understanding how risk assessment can be appropriately used in the site remediation process lies in understanding the strengths, limitations and uncertainties inherent in the characterization of risk. While risk assessment is an analytic process that is firmly based on scientific considerations, it also requires judgments to be made when available data and information is incomplete. These judgments or "assumptions" inevitably draw on both scientific and policy considerations which result in the introduction of uncertainty.

The risk estimates generated for the characterization of Chapter 21E disposal sites are usually not fully probabilistic estimates of risk but rather conditional point estimates. These estimates are prone to scientific uncertainty resulting from limitations in available data and the assumptions made in the absence of data. The risk estimates generated in *many* risk assessments (the *Residential ShortForm* being a typical example) are not measures of actual or absolute risks, but are generally intended to represent upper-bound (or high) estimates which are unlikely to underestimate the actual risk. The actual risk to a hypothetical receptor may be as high as the risk estimate, but is likely to be much lower. Thus, it is important to fully discuss the assumptions and uncertainties in any risk assessment to place risk estimates in perspective and aid in risk management decisions. Another use of an uncertainty analysis is to identify areas where a moderate amount of additional data collection might significantly improve the risk assessment process and thus improve the basis for selecting remedial alternatives.

The purpose of the uncertainty analysis is to document major assumptions and limitations and, if possible, provide an indication of whether they have resulted in an over- or under-estimation of risk. The uncertainty analysis may be qualitative, quantitative or both. Types of uncertainty analyses and the information they provide is discussed below.

11.2 Sources Of Uncertainty

According to the National Research Council (NRC, 1983), the uncertainties inherent in risk assessment can be grouped in two general categories: (1) missing or ambiguous information on a particular substance, and (2) gaps in current scientific theory. These uncertainties will exist in each step of the risk assessment process. In terms of site risk assessments, the sources of uncertainty can be broken into a number of components:

- uncertainty in the chemical monitoring data used to characterize exposure point concentrations;
- uncertainty in the environmental parameter measurements;
- uncertainty in the models used to evaluate contaminant transport and fate and to estimate exposure point concentrations in the absence of monitoring data;
- uncertainty associated with the exposure assessment including estimating frequency, duration and magnitude of exposure and with assigning exposure parameters to a non heterogenous population;
- uncertainty in the risk characterization process which reflects errors or uncertainties introduced through combination of the above sources of uncertainty.

Finally, additional uncertainties are incorporated in the risk assessment when exposure to multiple substances across multiple pathways are summed. A more complete discussion of these sources of uncertainty appears below.

Uncertainty in site characterization and site sampling data can stem from the error inherent in the sampling and analysis procedures, from a failure to take an adequate number of samples to arrive at sufficient characterization of the type and quantity of OHM released at or from the site, from mistakes on the part of the sampler, from the heterogeneity of the matrix being sampled, or from intentional bias in sample collection.

Environmental parameter measurements primarily contribute to uncertainty due to their absence. Lack of site-specific measurements dictates that estimates must be made based on literature values, regression equations, extrapolations, and best professional judgment.

In the absence of site specific sampling or environmental parameter measurements models are often used to predict exposure point concentrations and exposure doses. Modeling error arises primarily from the use of an inappropriate model or the use of an appropriate model but with inappropriate boundary conditions. A further limitation in modeling is that a model can only approximate reality. Other model errors can stem from a lack of validation or verification of the models.

The dose-response assessment is often one of the largest sources of uncertainty in any risk assessment. As noted by EPA in its Risk Assessment Guidance Document for Superfund Sites (U.S. EPA, 1989a):

Toxicity information for many of the chemicals found at disposal sites is often limited. Consequently, there are varying degrees of uncertainty associated with the toxicity values calculated. Sources of uncertainty include:

- using dose-response information from effects observed at high doses to predict the adverse health effects that may occur following exposure to the low levels expected from human contact with the agent in the environment;
- using dose-response information from short-term exposure studies to predict the effects of long-term exposures, and vice-versa;
- using dose-response information from animal studies to predict effects in humans; and
- using dose-response information from homogeneous animal populations or healthy human populations to predict the effects likely to be observed in the general population consisting of individuals with a wide range of sensitivities.

In addition to the uncertainties in dose-response values (such as the Reference Dose or Carcinogenic Potency Value), the Relative Absorption Values (RAFs) may also be a source of uncertainty.

The exposure assessment also introduces a number of uncertainties into the risk assessment process, particularly in the development of exposure point concentrations and the quantification of exposure parameters, many of which are not directly observable (e.g., frequency and duration of exposure). Exposure is in part based on the behavior patterns and personal habits of the exposed populations. Variations in human behavior thus represent a major source of uncertainty. There is also uncertainty associated with assigning point-estimates to exposure parameters such as body weight, ventilation rates and surface areas which are best described as distributions.

By definition, risk is a function of both exposure and toxicity. Thus, if either or both exposure or toxicity information are not accurate, risk estimates may not accurately reflect the potential risk.

In addition to the uncertainty that exists in evaluating the risk from single chemicals, further uncertainty is introduced in evaluating exposure and risk to multiple chemicals or mixtures. At most disposal sites, a mixture of chemicals is present in each media. To assess the overall effects of multiple chemicals, EPA developed "Guidelines for the Health Risk Assessment of Chemical Mixtures" (U.S. EPA, 1986). This guidance states that if sufficient data are not available on the effects of the chemical mixture of concern, or a reasonably similar mixture, the proposed approach is to assume additivity. This assumption, according to EPA, is expected to yield generally neutral risk estimates (i.e.,

neither conservative nor lenient). More recent guidance (U.S. EPA, 1989a) also references the "Guidelines for the Health Risk Assessment of Chemical Mixtures", but further states that the assumption of additivity assumes independence of action and that if this assumption is incorrect, over- or under-estimation of the actual multiple substance risk could result.

The impact of uncertainty on risk estimates and methods for evaluating uncertainty are discussed below.

11.3 Impacts Of Uncertainty On Risk Estimates

Historically, most disposal site risk assessments only provided a qualitative discussion of uncertainty. Usually, the discussion focused on a general discussion of the various sources of uncertainty discussed in Section 11.2, but provided very little information as to the relative impact of the various sources of uncertainty on the resultant site specific risk estimates.

It is well accepted in the field of environmental risk assessment that uncertainty about numerical risk estimates is generally large (i.e., an order of magnitude or greater). Given this level of uncertainty, it is important to focus on identifying the key site-related variables and assumptions that contribute most to uncertainty. To account for uncertainty and determine which factors most affect risk estimates, several approaches have been applied.

Rather than present a single point estimate representative of either an "average" or "maximum" exposure, risk assessments often present more than one risk estimate, each reflecting a combination of input values taken from the theoretical range of values for each parameter. The risk assessment results then include a range of risk estimates thought to place bounds on the risk.

The benefit of this approach is that while no one value may be thought to reflect actual exposure or risk, there is confidence that the "real risks" lay somewhere within the bounds of the risks presented. In some instances, the use of a range of risk estimates representing average and "worst case" exposure may be further evaluated by performing a sensitivity analysis. In a sensitivity analysis, the range of parameters suspected of driving the risks are varied and the corresponding degree to which changes in risk estimates occur can be described.

Even when a range of point estimates is presented, it is important to recognize that most risk assessments currently do not quantitatively deal with uncertainty. Because the risk assessment is based on a combination of uncertain point estimates for input values, the uncertainty in the final risk estimates reflects the accumulation of uncertainty in the assessment process.

For many of the factors which go into characterizing risks, point estimates may not be realistic, depending on the input values that are used. To account for this uncertainty, an alternate approach is to look at the distribution of many of these factors rather than rely on point estimates. The use of such probability distributions may provide a more realistic prediction of site risk.

Recently, methodologies for performing quantitative uncertainty analyses in public health risk assessments using Monte Carlo techniques have been developed. These approaches utilize distributions of values for key input parameters such as exposure point concentrations or exposure parameters while identifying distributions of risk values. Overall, the technique provides a quantitative means for estimating the probability distributions for health risks given the available information. These techniques can be used to "replace" the traditional point estimate risk assessment approach, or as an uncertainty analysis technique to evaluate point estimates.

In Monte Carlo type analyses, a range of risk is presented in terms of probability distributions. Using appropriate statistical summaries of the results, one can identify "mean" risk values, "median" risk values, and risk values at various percentiles of the distribution. This type of analysis enables risk managers to evaluate the risk assessment tool and its point estimates in terms of the risk management philosophy desired. This type of analysis has shown that typical health risk assessment methods produce very conservative point estimates (Burmaster, 1991; Finkel, 1990; Hawkins, 1991; McKone, 1991b; Roseberry, in press).

11.4 Just How Conservative Are We?

To be protective of human health and the environment, most risk assessments make assumptions that are very conservative and sometimes "worst case". The effect of combining multiple conservative input values in exposure and risk calculations is the development of very conservative "point estimates" of risk. In many cases, these very conservative "point estimates" overestimate the risks for a large majority of the population evaluated. In some cases, these point estimates may be overestimates for virtually the entire population (more than 99.99 % of the population). Such extremely conservative risk estimates may result in unnecessary public concern or unnecessarily expensive mitigation.

Work is currently underway to quantitatively assess the uncertainty in the *Residential ShortForm* process. In particular, an attempt will be made to put the *ShortForm* point estimates in perspective in order to evaluate the appropriateness of the standardized exposure and toxicity input values given the Bureau of Waste Site Cleanup's risk management philosophy.

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APPENDIX A

GLOSSARY OF TERMS AND ACRONYMS

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GLOSSORY OF TERMS & ACRONYMS

ADD	Average Daily Dose of a contaminant received by a receptor of concern (units of mg/kg/day)
ADE	Average Daily Exposure
ADSCR	Average Daily Soil Contact Rate (mg _{soil} /kg/day)
ADSIR	Average Daily Soil Intake Rate (mg _{soil} /kg/day)
AF	Fraction of OHM in soil absorbed through the skin (unitless)
AIC	Allowable Intake, Chronic
AIS	Allowable Intake, Subchronic
AP	Averaging Period (units: days)
ATC	Allowable Threshold Concentration (in air)
Background	The level of oil or hazardous material in the environment which would exist in the absence of the disposal site
BAF	Bioavailability Adjustment Factor (unitless), now called a Relative Absorption Factor
BW _{avg}	Average Body Weight of the receptor of concern during the period of exposure (units: mass)
C	Appropriate units conversion factor
c.21E	Massachusetts Law Chapter 21E, The Massachusetts Oil and Hazardous Material Release Prevention and Response Act.
CAG	U.S. EPA's Carcinogen Assessment Group
Cancer Risk Multiplier	A factor which combines food consumption parameters and plant uptake factors.
Carcinogenic Potency Value	Upper 95% Confidence Limit of the slope of the dose-response curve extrapolated to low doses.
CHIM	Chronic Hazard Index Multiplier

Chronic Hazard Index Multiplier	A factor which combines food consumption parameters and plant uptake factors for the evaluation of non-cancer health impacts from chronic exposures.
CPV	Carcinogenic Potency Value
CRM	Cancer Risk Multiplier
D ₁	Average duration of each exposure event (units: hours/event)
D ₂	Duration of the exposure period (units: days)
DAQC	The Massachusetts DEP Division of Air Quality Control: (617) 292-5630.
DEP	The Massachusetts Department of Environmental Protection
DEQE	The Massachusetts Department of Environmental Quality Engineering (former name of the MA DEP)
Disposal Site	Any structure, well, pit, pond, lagoon, impoundment, ditch, landfill or other place or area, excluding ambient air or surface water, where uncontrolled oil or hazardous material has come to be located as a result of any spilling, leaking, pouring, abandoning, emitting, emptying, discharging, injecting, escaping, leaching, dumping, discarding, or otherwise disposing of such oil or hazardous material. The term shall not include any site containing only oil or hazardous materials which: are lead-based paint residues emanating from a point of original application of such paint; resulted from emissions from the exhaust of an engine; are building materials still serving their original intended use or emanating from such use; or resulted from release of source, by-product or special nuclear material from a nuclear incident, as those terms are defined in 42 U.S.C.s.2014, if such release was subject to requirements with respect to financial protection established by the Nuclear Regulatory Commission under 42 U.S.C.s.2210. <u>A Disposal Site requires a Remedial Response Action.</u>
Dose	The amount of a substance, expressed in mg/kg body weight/day, which is absorbed into the body as a result of exposure(s).

DWPC	The Massachusetts DEP Division of Water Pollution Control: (617) 292-5673.
DWS	The Massachusetts DEP Division of Water Supply: (617) 292-5770.
ELCR	Excess Lifetime Cancer Risk
Environment	Waters, land, surface or subsurface strata, or ambient air of the Commonwealth
EP	Exposure Point
EPA	The United States Environmental Protection Agency
EPC	Exposure Point Concentration
Excess Lifetime Cancer Risk	The estimated probability that an individual's exposure, during a lifetime, to an oil or hazardous material would result in cancer.
Exposure	Any contact with or ingestion, inhalation, or assimilation of oil or hazardous materials, including irradiation. Also, the amount of material contacted and available for absorption.
Exposure Point	The place at which a human or environmental receptor is exposed to an oil or hazardous material
Exposure Point Concentration	The concentration of an oil or hazardous material in a specific medium at an exposure point.
F	Average number of events/day during the period of exposure (units: events/day)
FI	Daily intake of contaminated food on days exposed during the exposure period (units: mass/event)
Hazard Index	A calculation of the possibility of non-cancer health effects as the result of exposure to one or more oil or hazardous materials with similar modes of toxic action. The Hazard Index (HI) is defined as $HI = D_1/AD_1 + D_2/AD_2 + \dots D_i/AD_i$ where D is the daily dose for a particular oil or hazardous material, and AD is the allowable daily dose for a particular oil or hazardous material. The allowable daily dose is the Reference Dose or other allowable daily dose specified by the Department.

Hazardous Material	Material including, but not limited to, any material in whatever form which, because of its quantity, concentration, chemical, corrosive, flammable, reactive, toxic, infectious or radioactive characteristics, either separately or in combination with any substance or substances, constitutes a present or potential threat to human health, safety, welfare, or to the environment, when improperly stored, treated, transported, disposed of, used, or otherwise managed. The term shall not include oil, but shall include waste oil and all those substances which are included under 42 U.S.C.s.9601(14), but it is not limited to those substances. The term shall include but should not be limited to, all materials regulated as hazardous waste or regulated recyclable materials pursuant to 310 CMR 30.000.
HI	Hazard Index
I	Daily soil ingestion rate on days exposed during the exposure period (units: mass/day)
IARC	The International Agency for Research on Cancer
IM	Interim Measure
Imminent Hazard	A hazard which would pose a significant or otherwise unacceptable risk of harm to health, safety, public welfare or the environment if it were present for even a short period of time.
Interim Measure	A category of actions which may be implemented at M.G.L. c.21E disposal sites according to the MA DEP Bureau of Waste Site Cleanup policy # WSC-131-90.
IRIS	The US EPA's Integrated Risk Information System
LADD	Lifetime Average Daily Dose
LADSCR	Lifetime Average Daily Soil Contact Rate normalized to bodyweight (mg _{soil} /kg/day)
LADSIR	Lifetime Average Daily Soil Intake Rate normalized to bodyweight (mg _{soil} /kg/day)
Limit of Detection	Generally, the smallest concentration of a substance that can be reliably distinguished from background noise. Typically, the signal to noise ration is 3.
LOD	Limit of Detection
MA DEP	The Massachusetts Department of Environmental Protection

Massachusetts Contingency Plan	310 CMR 40.000
MCP	The Massachusetts Contingency Plan
MDL	Method Detection Limit
Media	Air, soil, or water
Method 3a	A single-medium risk characterization conducted under the MCP pursuant to 40.545(3)(g)3.a.
Method 3b	A multi-media risk characterization conducted under the MCP pursuant to 40.545(3)(g)3.b.
Method Detection Limit	Generally, the level which can be measured with 99% accuracy using EPA Standard Methods.
Migration Pathway	A pathway by which an oil or hazardous material is transported at or from a disposal site.
MS	Mass of soil in contact with unit surface area of skin (units: mass/area)
Multi-media	The most common contamination scenario. A disposal site where exposure is thought to occur via more than one exposure medium.
MW	Molecular Weight
ND	Not Detected
NFA	No Further Action
NOAEL	The No Observable Adverse Effects Level
NRC	National Research Council
OHM	Oil or Hazardous Material
Oil	Insoluble or partially soluble oils of any kind or origin or in any form, including, without limitation, crude or fuel oils, lube oil or sludge, asphalt, insoluble or partially insoluble derivatives of mineral, animal or vegetable oils. The term shall not include waste oil, and shall not include those substances which are included in 42 U.S.C.s. 9601(14).

Permanent Solution	A measure or combination of measures which will, when implemented, ensure attainment of a level of control of each identified substance of concern at a disposal site or in the surrounding environment such that no substance of concern will present a significant or otherwise unacceptable risk of damage to health, safety, public welfare, or the environment during any foreseeable period of time.
Phase II	The Comprehensive Site Assessment phase of the Massachusetts Contingency Plan
Phase III	The Evaluation of Remedial Response Alternatives and the Final Remedial Response Plan phase of the Massachusetts Contingency Plan.
Potency Value	US EPA's Cancer Assessment Group's published cancer slope value
Potentially Responsible Party	Any person who is potentially liable pursuant to MGL c. 21E (PRP)
ppb	Parts Per Billion
ppm	Parts Per Million
PQL	Practical Quantitation Limit
Practical Quantitation Limit	Generally, the smallest concentration of a substance for which <u>quantitative</u> results may be obtained with a specified degree of confidence.
PRP	A Potentially Responsible Party
q ₁	U.S. EPA's Cancer Assessment Group's published cancer slope value
RAF	Relative Absorption Factor
Receptors	Individual or environmental population exposed to oil or hazardous materials.
Reference Concentration	The concentration in air of an oil or hazardous material which would not be expected to result in any adverse non-cancer health effects as published by the U.S. EPA.
Reference Dose	The daily dose of an oil or hazardous material which would not be expected to result in any adverse non-cancer health effects as published by the U.S. EPA.

Relative Absorption Factor	A factor which adjusts the dose estimate in consideration of the absorption efficiencies of the study which is the basis of the toxicity information and the absorption efficiency of the route of exposure of concern. It is not itself an absorption efficiency. This term was formerly called a "Bioavailability Adjustment Factor" by the Department.
Release	Includes any spilling, leaking, pumping, pouring, emitting, emptying, discharging, injecting, escaping, leaching, dumping or disposing into the environment, but excludes: (1) emissions from the exhaust of an engine; (2) release of source, by-product, or special nuclear material from a nuclear incident, as those terms are defined in 42 U.S.C.s.2014, if such release is subject to requirements with respect to financial protection established by the Nuclear Regulatory Commission under 42 U.S.C.s 2210; (3) the normal application of fertilizer; and (4) the application of pesticides in a manner consistent with their labeling.
Remedial Response Action	A response action at a Location To Be Investigated (LTBI) or a disposal site that is taken pursuant to the Massachusetts Contingency Plan
Residential	Those disposal sites for which the current or reasonably foreseeable use has been determined to be residential, or those sites which are evaluated with the assumption that the use could be residential, or sites "surrounded" by residential properties.
RfC	Reference Concentration
RfD	The U.S. EPA's published Reference Dose
Route of Exposure	A mechanism, including, but not limited to ingestion, inhalation, dermal absorption, and transpiration by which an oil or hazardous material comes into contact with a human or environmental receptor.
RP	Respirable Particulates (units: mass)
SA	Skin surface area in contact with the contaminated soil on days exposed (units: area/day)
SHIM	Subchronic Hazard Index Multiplier
ShortForm	The Risk Assessment ShortForm, the spreadsheet risk assessment tool.
Short Term Measure	A measure or combination of measures that is taken pursuant to 310 CMR 40.542. See MA DEP Bureau of Waste Site Cleanup policy # WSC-130-90.

Single-Medium	Disposal sites where exposure is thought to occur via a single exposure medium, or where the nature of combined exposures indicates that a single medium-specific program within the MA DEP (DAQC, DWS) would normally address the problem.
Site	Any building, structure, installation, equipment, pipe or pipeline including any pipe discharging into a sewer or publicly-owned treatment works, well, pit, pond, lagoon, impoundment, ditch, landfill, storage container, motor vehicle, rolling stock, or aircraft, or any other place or area where oil or hazardous material has been deposited, stored, disposed of or placed, or otherwise come to be located. The term shall not include any consumer product in consumer use or any vessel.
STM	Short Term Measure
Subchronic Hazard Index Multiplier	A factor combining food intake parameters and plant uptake factors for subchronic exposures.
Substantial Hazard	A hazard which would pose a significant or otherwise unacceptable risk of harm to health, safety, public welfare, or the environment if it continued to be present for several years.
SVOC	Semi-Volatile Organic Compound
TEL	Threshold Effects Level (from CHEM, MA DEP 1990c)
Temporary Solution	A measure or combination of measures which will, when implemented, eliminate any substantial hazards posed by a priority disposal site until a permanent solution can be implemented.
Total Site Cancer Risk	The sum of the estimated excess lifetime cancer risks associated with exposure to all oil and hazardous materials at or from a disposal site at all exposure points for a given receptor.
Total Site Noncancer Risk	A calculation of the possibility of non-cancer health effects associated with exposure to all oil and hazardous materials at or from a disposal site at all exposure points for a given receptor. The Hazard Index is a measure of the Total Site Non-Cancer Risk.
UF	Uncertainty Factor
Unit Risk	The Upper 95% Confidence Limit of the lifetime cancer risk estimated to result from lifetime exposure to a unit concentration of an agent.

UR	Unit Risk Value
VI	Daily volume of drinking water ingested by the receptor of concern at the exposure point during the exposure period (units: volume/day)
VM	Daily volume of mother's milk ingested by the infant during the exposure period (units: volume/day)
VOC	Volatile Organic Compound
VR	Daily respiratory volume for the receptor of concern during the period of exposure (units: volume/day)
[X],	Concentration of substance "X" in medium "y"

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APPENDIX B

TOXICITY PROFILES

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APPENDIX B - TOXICITY PROFILES

This appendix contains a Toxicity Profile (or Summary) for each of the substances contained in the *Residential ShortForm*.

The MCP Phase II Risk Characterization Report should contain a Toxicity Profile for each of the chemicals reported at the disposal site. As described in Section 4.4, these Profiles serve several purposes, including educating the public about potential hazards associated with the chemicals and serving as a basis for the quantitative risk characterization.

The Toxicity Profiles contained in this Appendix may be copied and submitted as part of the Phase II Report. These Profiles will be periodically updated, and the risk assessor should insure that the most current version is used.

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ACENAPHTHENE

GENERAL BACKGROUND INFORMATION

Acenaphthene is a member of the polycyclic aromatic hydrocarbons (PAH). PAHs are a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. The database for acenaphthene is very limited.

PHARMACOKINETICS

No data were found regarding the pharmacokinetics of acenaphthene.

HUMAN TOXICOLOGICAL PROFILE

No data were found regarding the human toxicology of acenaphthene.

MAMMALIAN TOXICOLOGICAL PROFILE

Adverse effects on the lungs, glands, and blood were observed in rats following aerosol administration of 12 mg/m³ acenaphthene for 5 months (U.S. EPA, 1981).

GENOTOXICITY

Mutagenicity tests for acenaphthene were negative (U.S. EPA, 1981). Carcinogenicity tests were negative (IARC, 1983).

REFERENCES

International Agency for Research on Cancer (IARC) (1983) *Monograph on the evaluation of carcinogenic risk of chemicals to man: polynuclear aromatic hydrocarbons*. 32:33-43.

U.S. Environmental Protection Agency (U.S. EPA) (1981) An exposure and risk assessment for acenaphthalene. U.S. EPA Contract No. 68-01-6017. Office of Water Regulations and Standards, Washington, D.C.

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ACENAPHTHYLENE

GENERAL BACKGROUND INFORMATION

Acenaphthylene is a member of the polycyclic aromatic hydrocarbons (PAH). PAHs are a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. The data on acenaphthylene are limited.

PHARMACOKINETICS

No data were found regarding the pharmacokinetics of acenaphthylene.

HUMAN TOXICOLOGICAL PROFILE

No data were found regarding the human toxicity of acenaphthylene.

MAMMALIAN TOXICOLOGICAL PROFILE

No data were found regarding the mammalian toxicity of acenaphthylene.

GENOTOXICITY

Data from a single mutagenicity assay using acenaphthylene were positive (U.S. EPA, 1982).

REFERENCES

U.S. Environmental Protection Agency (U.S. EPA) (1982) An exposure and risk assessment for polynuclear aromatic hydrocarbons (acenaphthylene). U.S. EPA Contract 68-01-6017. Office of Water Regulations and Standards. Washington, D.C.

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ANTHRACENE

GENERAL BACKGROUND INFORMATION

Anthracene is a polycyclic aromatic hydrocarbon (PAH). PAHs are a class of compounds which are non-polar and contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. As a PAH, anthracene is found in tobacco smoke, certain foods, and the emissions from industrial or natural burning.

PHARMACOKINETICS

Little data were found regarding the pharmacokinetics of anthracene. The intestinal absorption of anthracene is less dependent on the presence of bile in the stomach than is the absorption of larger PAHs such as benzo(a)pyrene (Rahman et al, 1986).

HUMAN TOXICOLOGICAL PROFILE

Anthracene is a skin irritant and allergen (Sax, 1984). Humans exposed to anthracene in an occupational setting may demonstrate skin disorders (Clement, 1985). Anthracene has been associated with gastrointestinal tract toxicity in humans (Badiali et al, 1985). However, the usefulness of this study is limited due to confounding factors. Hematopoietic toxicity has also been observed in cancer patients who have been treated with anthracene-containing chemotherapeutics (Falkson et al, 1985). No control groups and concomitant exposure to other ingredients in the therapeutic agents prevents any definitive conclusions.

MAMMALIAN TOXICOLOGICAL PROFILE

A subchronic study where anthracene was administered to mice by gavage for at least 90 days found no treatment-related effects at doses up to 1000 mg/kg-day (USEPA, 1989).

The data on the carcinogenicity of anthracene are considered inadequate by EPA (IRIS, 1991).

GENOTOXICITY

Tests for DNA damage, mutation, chromosome effects and cell transformation in a variety of eukaryotic cell preparations have shown negative results. The majority of tests using anthracene in prokaryotes are negative, but positive results are reported in one or two tests (ATSDR, 1990; IRIS, 1991).

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ARSENIC

GENERAL BACKGROUND INFORMATION

The toxicity of arsenic depends upon its chemical form along with the route, dose, and duration of exposure. In general, arsenites (As^{+3}) are potentially more toxic than arsenates, soluble arsenic compounds are potentially more toxic than insoluble compounds, and inorganic arsenic compounds are potentially more toxic than organic derivatives (U.S. EPA, 1985).

PHARMACOKINETICS

Absorption from the gastrointestinal tract is dependent upon the solubility of the specific arsenic compound and the dose. Absorption from the respiratory tract is also dependent upon the specific arsenic compound, along with particle size (see section on Relative Absorption Factors).

HUMAN TOXICOLOGICAL PROFILE

Depending upon dose and exposure route, arsenic is an irritant of the skin, mucous membranes, and the gastrointestinal tract. Acute toxicity from the ingestion of higher doses of arsenic may result in vomiting, diarrhea, convulsions, a severe drop in blood pressure, and cardiovascular effects. The lethal dose for humans is reported to be 1.0 to 2.6 mg/kg-bw (Vallee et al., 1960). Acute toxicity from inhalation exposure to arsenic adsorbed to particulate matter may result in conjunctivitis and pharyngitis. Subchronic effects included hyperpigmentation (melanosis), multiple arsenical keratoses, sensory-motor polyneuropathy, persistent chronic headache, lethargy, gastroenteritis, and mild iron deficiency anemia. Inhaled arsenic compounds have been reported to be associated with skin lesions, cardiovascular and respiratory effects, and peripheral neuropathy (Stokinger, 1981; IARC, 1980). Chronic oral exposure of humans to inorganic arsenic compounds has been reported to cause skin lesions, peripheral vascular disease, and peripheral neuropathy (Silver and Wainman, 1952). The incidence of blackfoot disease, a peripheral circulatory disease characterized by gangrene of the extremities, has reportedly been related to the presence of arsenic in the drinking water of residents of the southwest of Taiwan (Tseng, 1977). The symptoms of chronic inhalation exposure to arsenic compounds are similar to those associated with chronic oral toxicity.

MAMMALIAN TOXICOLOGICAL PROFILE

Oral LD₅₀ values for trivalent arsenic vary from 15 to 293 mg/kg in rats and from 10-150 mg/kg in other test species (U.S. EPA, 1984). Chronic toxicity data from arsenic exposure to rats cannot be extrapolated to man as the rat is able to store this compound bound to hemoglobin in red blood cells (Lanz et al., 1950). This binding results in extremely slow excretion by rats compared to other species (Mealey et al., 1959). For this reason, dogs have been used to obtain experimental toxicity information. Studies of the subchronic oral toxicity of diets containing sodium arsenite or sodium arsenate in dogs report that arsenite is potentially more toxic than arsenate. The NOEL (no observed effect level) was reported to be 50 mg/kg-diet for both substances (Byron et al., 1967). Schroeder and Balassa (1967) studied the chronic oral toxicity of arsenic on growth and survival in mice. Ingestion of water containing As⁺³ at 5 mg/L over two years is reported to have resulted in decreased survival and reduced median life span in male and female mice. No information regarding chronic inhalation exposure of experimental animals to arsenic could be located in the available literature. Animal studies to test the teratogenic potential of arsenic have been performed. Matsumoto et al. (1973) reported decreased fetal weight in oral doses of up to 40 mg-arsenate/kg-bw/day administered to pregnant mice for three consecutive days. Diets containing up to 100 mg-arsenite/kg-diet, however, were reported to have had no effect on offspring (Kojima, 1974). No data regarding the teratogenicity of inhaled arsenic could be found in the literature.

GENOTOXICITY

Nearly all results of gene mutation studies for arsenic (III) and arsenic (V) compounds have been negative. Arsenite and arsenate also have been inactive in gene-specific mutation assays in yeast and in cultured mammalian cells. In contrast, arsenic (III), arsenic (V), arsenite and arsenate have been found to result in chromosome aberrations and sister chromatid exchanges in cultured animal and human cells tested in vitro (ATSDR, 1987). There is limited evidence that occupational exposure to arsenic may cause chromosome changes in humans (Beckman et al., 1977). Beckman et al. (1977) reported an increase in gaps, chromatid aberrations and chromosome aberrations from mine workers at a smelter in northern Sweden.

The majority of tests in which experimental animals were exposed orally to a variety of arsenic compounds produced negative results regarding carcinogenicity (Hueper and Payne, 1962; Byron et al., 1967). A few studies have, however, reported tumorigenic effects of arsenic treatment (Schrauzer et al., 1978). Mixed results were reported in arsenic inhalation studies (Ishinishi et al., 1977; Ivankovic et al., 1979). Epidemiological studies conducted in the U.S. have failed to correlate the incidence of skin cancer with arsenic in drinking water (Morton et al., 1976; Goldsmith et al., 1972). A dose-response relationship between the

occurrence of skin cancer and arsenic consumption in the drinking water of Taiwanese, however, was reported by Tseng et al. (1977). Arsenic exposure at certain doses may produce a pattern of skin disorders, hyperpigmentation, and keratosis that may develop into basal or squamous cell carcinoma (U.S. EPA, 1985). Several epidemiological studies of workers occupationally exposed to arsenic have reported a correlation between this exposure and mortality due to respiratory cancer (Higgins et al., 1982; Enterline and Marsh, 1982; Brown and Chu, 1983). Based upon epidemiological data, the EPA has classified arsenic as Group A -Human Carcinogen.

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BENZENE

GENERAL BACKGROUND INFORMATION

Benzene is a clear, volatile, highly flammable, aromatic hydrocarbon which exists naturally and is produced by volcanoes and forest fires. Benzene is also a very common industrial solvent, produced from petroleum. It is used as a solvent for fats, inks, paints, plastics, rubber, in the extraction of oils from seeds and nuts, in photogravure printing, as a chemical intermediate and in the manufacture of detergents, explosives, pharmaceuticals and dyestuffs. It is also a component of gasoline and other petroleum-based fuels. Exposure to benzene can occur via inhalation, ingestion, especially of contaminated drinking water, and dermal contact (as in contact with liquid benzene found in gasoline.) (Sittig, 1981; ATSDR, 1989)

PHARMACOKINETICS

Benzene is readily absorbed through ingestion, moderately absorbed through inhalation and poorly absorbed through intact skin (see section on Relative Absorption Factors). Once in the bloodstream, benzene is distributed throughout the body, with the concentration in any one compartment dependent on the degree of perfusion of tissues by blood. Since benzene is lipid-soluble, it accumulates in fat, but the rate of accumulation is slow since fat is poorly perfused. The metabolites of benzene are responsible for its toxic effects. These include phenol (which is either formed via an unstable benzene oxide precursor or directly from benzene), catechol, hydroquinone and conjugated phenolic compounds. The primary site of benzene metabolism is the liver via the cytochrome P450 mixed function oxidase system. Some benzene metabolism may also occur in the bone marrow via the same enzyme system. Benzene is excreted either unchanged from the lungs or as metabolites in the urine (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Benzene targets its effects on the hemopoietic, immune and nervous systems (ATSDR, 1989). Exposure to benzene has produced irritation of the skin, eyes and upper respiratory tract. Acute exposure has produced central nervous system depression, headache, dizziness, nausea, convulsions, coma and death at extremely high concentrations (Sittig, 1981). Health effects in humans have been reported starting as low as 50 ppm via inhalation. Twenty-five ppm for 6 hrs had no obvious effects though benzene was detected in blood (Sandmeyer, 1981). Early autopsy reports found benzene-induced hemorrhages of the brain, pericardium, urinary tract, mucous membranes and skin (Sittig, 1981). Chronic exposure to benzene produces blood changes involving an initial increase in levels of erythrocytes, leukocytes and

thrombocytes, followed by aplastic anemia indicated by anemia, leukopenia and thrombocytopenia (Sittig, 1981).

MAMMALIAN TOXICOLOGICAL PROFILE

The following effects have been produced experimentally in laboratory animals, following exposure to benzene: decreased leukocyte and/or erythrocyte counts, reduction in cellular immunity and bone marrow depression (reduced number of granulopoietic stem cells). Animal studies do not indicate that benzene is teratogenic, but the following fetotoxic effects have been found: reduced fetal weight, altered fetal hematopoiesis, fetal skeletal variations and increased resorptions in pregnant exposed animals. In addition, benzene has produced histopathological changes in ovaries and testes of test animals (ATSDR, 1989).

GENOTOXICITY

Benzene and its metabolites have been shown to be mutagenic in a number of in vitro and in vivo studies. Genotoxic effects produced experimentally include structural and numerical chromosome aberrations in humans, animals and cell cultures, and sister chromatid exchanges and micronuclei in in vivo animal studies. Benzene exposure has been found to produce an increase in the number of chromosome aberrations associated with myelotoxicity (Sittig, 1981). In addition, sperm head abnormalities, inhibition of DNA and RNA synthesis, DNA binding and interference with cell cycle progression have been shown in in vitro studies (ATSDR, 1989). The epidemiologic data indicate that benzene is leukemogenic. The evidence is most convincing for acute myelogenous and acute erythroleukemia, although a correlation has also been found with chronic leukemia. Benzene has been designated a group A human carcinogen (leukemogen) by inhalation. Although data are insufficient to validate the carcinogenicity of benzene via ingestion, it would not be unreasonable that benzene is carcinogenic via this route as well if present in sufficient quantities. The carcinogenicity of benzene via dermal exposure is considered to be lower since benzene is absorbed poorly through the skin (ATSDR, 1989).

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BENZO[a]ANTHRACENE

GENERAL BACKGROUND INFORMATION

Benzo[a]anthracene (BaA) is a member of the polycyclic aromatic hydrocarbons (PAH). PAHs are a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. The overall database for benzo[a]anthracene is limited. Human exposures to BaA can come from the oral, inhalation or dermal routes. BaA is produced when gasoline or other organic material is burned. It is also found in cigarette smoke and cooked food. People most at risk from exposure to BaA are those in the coal tar and asphalt production industries, cooking plants, coal gasification plants, smoke houses and industrial plants that burn wood, trash, coal or oil.

PHARMACOKINETICS

BaA is absorbed by the dermal and oral routes. There is no information on absorption by inhalation. Biotransformation to reactive intermediates is necessary for toxicity (ATSDR, 1990). BaA accumulates in adipose tissue. The metabolism of BaA is similar to the metabolism of benzo[a]pyrene (Cooper et al., 1983). In brief, the aromatic ring is oxidized by arene oxides to form reactive intermediates. The reactive intermediates are subsequently hydrolyzed to diols (Sims and Grover, 1974). The diols are conjugated with glutathione and excreted.

HUMAN TOXICOLOGICAL PROFILE

There are no reports directly correlating human exposure to BaA with the development of excess tumors.

MAMMALIAN TOXICOLOGICAL PROFILE

The only toxicity endpoint that has been adequately studied for BaA is dermal carcinogenicity. There is some evidence that benz[a]anthracene is carcinogenic in laboratory animals by the oral route (Klein, 1963; Bock and King, 1959) and also by subcutaneous injection (IARC, 1973). BaA has been shown to cause skin tumors after dermal application (Bingham and Falk, 1969). Tumorigenicity of the diol epoxide metabolite has been shown (Levin et al., 1978) as well as the mutagenicity of the diol epoxide (Wood et al., 1977).

GENOTOXICITY

The metabolism of BaA is an essential event in producing genotoxic effects in both *in vitro* and *in vivo* biological test systems (ATSDR, 1990). The intermediates formed by BaA metabolism are reactive electrophiles which are capable of interacting with DNA.

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BENZO[a]PYRENE

GENERAL BACKGROUND INFORMATION

Benzo[a]pyrene (BaP) is a member of the class of compounds generally referred to as polyaromatic hydrocarbons (PAH).

PAHs contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. BaP is a component of fossil fuels and is produced from the incomplete combustion of organic compounds. BaP and other PAHs are found in coal tar, creosote oils and pitches formed from the distillation of coal tars (ATSDR, 1990).

PHARMACOKINETICS

BaP is readily absorbed by dermal, inhalation and oral routes (see section on Relative Absorption Factors). Distribution of BaP is rapid among several tissues. Following inhalation exposure to ³H labeled BaP, maximum levels of radioactivity were found in the liver, esophagus, small intestine and blood after 30 minutes. After 12 hours, maximum levels were found in the cecum, stomach and large intestine (Sun et al., 1982). This and other studies provide evidence for the enterohepatic circulation of BaP metabolites.

Mammalian metabolism of BaP follows the mechanism established for smaller aromatic compounds (Williams, 1959). There is an initial oxidation of a double bond on one of the rings to an arene oxide. The oxide is then hydrolyzed to the diol. Oxidations may occur at multiple sites on the BaP molecule. Phase II metabolism is considered the detoxication pathway and involves the conjugation of the activated Phase I metabolites with easily eliminated substrates such as glutathione, glucuronide or sulfate (Cooper et al., 1983). In addition to being conjugated, the diol intermediate can undergo (1) further oxidation to several uncharacterized metabolites via the P-450 monooxygenase system, (2) spontaneous rearrangement to the phenol or (3) hydration to the trans-diols through a reaction catalyzed by epoxide hydrolase (Cooper et al., 1983). BaP 7,8-diol-9,10-epoxide has been established as an ultimate carcinogen (ATSDR, 1990). The primary route of excretion of BaP is through the feces. BaP undergoes first-pass metabolism and is reabsorbed via enterohepatic circulation (Chipman et al., 1982). Rats exposed by gavage to ¹⁴C labeled BaP in peanut oil excreted up to 85% in the feces. Excretion in the urine was 1 to 3% of the administered dose (Hecht et al., 1979).

HUMAN TOXICOLOGICAL PROFILE

The database for the toxicological effects of BaP on humans, separate from PAHs, is limited. Toxic effects attributable to mixtures of PAHs include a variety of skin lesions and non-cancer lung diseases such as bronchitis (IARC, 1973).

MAMMALIAN TOXICOLOGICAL PROFILE

BaP is a moderately potent experimental carcinogen in numerous species by many routes of exposure (IARC, 1983). Mice exposed to doses of BaP ranging from 1.5 to 400 mg/kg/d developed benign and malignant tumors of the forestomach (Hartwell, 1951; Thompson, 1971). Acute intragastric doses of 50 to 67 mg/kg of BaP have been shown to elicit pulmonary adenomas and forestomach papillomas in mice (Sparnins et al., 1986; Wattenberg and Beuding, 1986). Intermittent gavage exposure of mice to 50 to 67 mg/kg BaP resulted in 100% forestomach and pulmonary tumor incidences at 30 weeks of age (Sparnins et al., 1986; Wattenberg and Leong, 1970). Mice fed BaP at concentrations equivalent to 33.3 mg/kg/d exhibited gastric neoplasms following two or more days of consumption. However, lower concentrations of BaP (equivalent to 13.3 mg/kg/d) administered for up to 7 days did not produce any forestomach tumors (Neal and Rigdon, 1967). Hamsters have developed papillomas and carcinomas of the alimentary tract following gavage or dietary exposure to BaP (Chu and Malmgren, 1965). A single oral dose of 100 mg BaP (200mg/kg) produced mammary tumors in 88% of female Sprague-Dawley rats (Huggins and Yang, 1962). A 77% mammary tumor incidence was observed 90 weeks after a single oral dose of BaP of 50 mg (100mg/kg) was administered to rats (McCormick, 1981).

GENOTOXICITY

There are no studies relating exposure to BaP in humans to genotoxicity. In short-term *in vitro* and *in vivo* genetic toxicology tests, BaP has been shown to be a potent genotoxic agent when metabolically activated. In mice, oral exposure to 10 mg/kg BaP produced gene mutations in the mouse coat color spot test (Davidson and Dawson, 1976,1977). BaP shows positive mutagenic activity, *in vitro*, in several strains of *Salmonella typhimurium* in the presence of either rodent microsomes or hepatocytes for exogenous metabolic activation (ATSDR, 1990). Epidemiological studies have shown increased incidences of lung cancer in humans exposed via inhalation to mixtures of PAHs which include BaP (ATSDR, 1990).

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BENZO[b]FLUORANTHENE

GENERAL BACKGROUND INFORMATION

Benzo[b]fluoranthene (BbF) is a member of the class of compounds referred to as polycyclic aromatic hydrocarbons (PAHs). PAHs contain two or more aromatic rings. PAHs are ubiquitous in nature and are both naturally occurring and man-made. Exposure to BbF can come from air, water, or soil. As a PAH, BbF is present in the emissions from industrial plants that produce coal tar, cooking plants, asphalt production plants, and home heating with wood and coal. BbF is also present in charcoal-broiled foods and cigarette smoke (ATSDR, 1990).

PHARMACOKINETICS

No data on the absorption, distribution or excretion of BbF were identified. BbF is metabolized under *in vitro* incubation conditions to phenol and dihydrodiol metabolites (Amin et al., 1982). The general metabolic pathways elucidated for benzo(a)pyrene are also active on BbF (Cooper et al., 1983; Levin et al., 1982; Grover et al., 1986). The reactive metabolites associated with the tumorigenic effects of BbF may not be the diol epoxides (Amin et al., 1982; Amin et al., 1985). As for the other PAHs, the material excreted is expected to consist primarily of dihydrodiol and phenol conjugates (Grover et al., 1986).

HUMAN TOXICOLOGICAL PROFILE

The database for human toxicity is very limited. There are no studies correlating exposure to BbF and cancer or systemic toxicity. The only data implicating BbF as a carcinogen come from carcinogenicity studies using a mixture of PAHs.

MAMMALIAN TOXICOLOGICAL PROFILE

The database on the toxicity of BbF is limited. Intratracheal administration of BbF to rats resulted in an increase in respiratory tract tumors (Deutsch-Wenzel et al., 1983). BbF has caused skin tumors in mice following dermal application (Wynder and Hoffman, 1959). The skin tumor initiating ability of BbF has been demonstrated in mice using a standard initiation/promotion protocol with either croton oil or phorbol myristate acetate as a tumor promotor (Amin et al., 1985; LaVoie et al., 1979, 1982).

GENOTOXICITY

The genotoxicity of BbF has been shown equivocally in three *in vitro* studies. BbF has been shown to be mutagenic in *Salmonella typhimurium* in the presence of an exogenous rat-liver preparation (LaVoie et al., 1979). Mutagenic activity has been reported in another similar study (Hermann, 1981). Negative results were reported by Mossanda (1979). The results cannot support an unequivocal determination regarding the genotoxicity of BbF at this time.

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BENZO[g,h,i]PERYLENE

GENERAL BACKGROUND INFORMATION

Benzo[g,h,i]perylene is a member of the polycyclic aromatic hydrocarbons (PAH). PAHs constitute a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. The data regarding benzo[g,h,i]perylene are limited. As a PAH, it is found in food (charcoal broiled meats), vegetables, tobacco smoke and soot (U.S. EPA, 1980). Exposure occurs by inhalation, ingestion and by dermal contact.

PHARMACOKINETICS

No data were found regarding the pharmacokinetics of benzo[g,h,i]perylene.

HUMAN TOXICOLOGICAL PROFILE

No data were found regarding the human toxicology of benzo[g,h,i]perylene.

MAMMALIAN TOXICOLOGICAL PROFILE

No data were found regarding the mammalian toxicity of benzo[g,h,i]perylene.

GENOTOXICITY

No data were found regarding the genotoxicity of benzo[g,h,i]perylene.

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BENZO[k]FLUORANTHENE

GENERAL BACKGROUND INFORMATION

Benzo[k]fluoranthene (BkF) is a member of the class of compounds referred to as polycyclic aromatic hydrocarbons (PAHs). PAHs contain two or more aromatic rings. PAHs are ubiquitous in nature and are both naturally occurring and man-made. Exposure to BkF can come from air, water, or soil. As a PAH, BkF is present in the emissions from industrial plants that produce coal tar, cooking plants, asphalt production plants, and home heating with wood and coal. BkF is also present in charcoal-broiled foods and cigarette smoke (ATSDR, 1990).

PHARMACOKINETICS

No data on the absorption, distribution or excretion of BkF were identified. BkF is believed to be metabolized to phenol and dihydrodiol metabolites (ATSDR, 1990). The general metabolic pathways elucidated for benzo[a]pyrene are believed to be active on BkF. As for the other PAHs, the material excreted is expected to consist primarily of dihydrodiol and phenol conjugates (Levin et al., 1982; Cooper et al., 1983; Grover et al., 1986).

HUMAN TOXICOLOGICAL PROFILE

The database for human toxicity is very limited. There are no studies correlating exposure to BkF and cancer or systemic toxicity. The only data implicating BkF as a carcinogen come from carcinogenicity studies using a mixture of PAHs.

MAMMALIAN TOXICOLOGICAL PROFILE

The database on the toxicity of BkF is limited. The skin tumor initiating ability of BkF has been demonstrated in mice using a standard initiation/promotion protocol with either croton resin or phorbol myristate acetate as tumor promoters (Van Duuren et al., 1966; LaVoie et al., 1982). Chronic dermal application of benzo[k]fluoranthene to mice resulted in no skin tumors, suggesting that BkF alone is not a complete carcinogen (Wynder and Hoffman, 1959).

GENOTOXICITY

The genotoxicity of BkF has not been documented in *in vitro* studies. In vivo, a single topical application of BkF was reported to bind to DNA in CD-1 mouse skin (Weyland et al., 1987). Covalent binding of chemicals to DNA can result in strand breaks and DNA damage, ultimately leading to mutations (ATSDR, 1990).

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BIS(2-ETHYLHEXYL)PHTHALATE

GENERAL BACKGROUND INFORMATION

Bis(2-ethylhexyl)phthalate, often referred to as Di(2-ethylhexyl)phthalate (DEHP), exists as a colorless, oily liquid at room temperature. It is used industrially as a plasticizer for resins, to make plastic materials more flexible. DEHP is contained in many plastic products such as imitation leather, rainwear, footwear and toys. It is used in the manufacture of tubing and containers used for blood transfusions and kidney dialysis. DEHP is also used in the manufacture of organic pump fluids in electrical capacitors. DEHP may migrate into the environment under improper use/disposal conditions. As a result, exposure could occur via air, water and food. Patients receiving blood transfusions or kidney dialysis can also be exposed to DEHP (ATSDR, 1989; Sittig, 1981).

PHARMACOKINETICS

DEHP is readily absorbed through ingestion and inhalation and poorly absorbed through the skin (see section on Relative Absorption Factors). DEHP is largely metabolized prior to intestinal absorption, via hydrolysis, to its corresponding monoester metabolite (MEHP), with the release of 2-ethylhexanol. Once absorbed, DEHP and its metabolites are distributed throughout the body, with most of the compounds initially going to the liver. In general, DEHP and its metabolites are converted to more polar derivatives and are then excreted. DEHP is rapidly cleared from the body, with little potential for accumulation. There are differences in the way DEHP is metabolized among species. Although phase I reactions are essentially the same across species except for quantitative differences, phase II reactions differ among species as to the ability to glucuronidate DEHP and its metabolites. The relationship between pharmacokinetics and toxicity is not known due to gaps in knowledge regarding mechanisms of toxic action (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Acute toxicity from DEHP is relatively low by both inhalation and ingestion. A 1-hr exposure to 23,670 mg/m³ DEHP did not result in any deaths. The oral LD50 for DEHP ranges from 26,000 to 49,000 mg/kg (ATSDR, 1989). Exposure to DEHP has produced irritation of the eyes, and mucous membranes, nausea and diarrhea (Sittig, 1981). Liver biopsies from dialysis patients showed liver abnormalities (peroxisome proliferation) (ATSDR, 1989). Most of the toxicity data for DEHP originate from animal studies.

MAMMALIAN TOXICOLOGICAL PROFILE

Laboratory studies indicate that DEHP targets the liver and the testes. DEHP, administered at high levels, has induced morphological and biochemical liver changes in a number of rodent studies. Both DEHP and MEHP, its metabolite, have also been shown to produce reduced organ weight and damage to the seminiferous tubules of the testes. DEHP has also produced developmental and reproductive effects in laboratory rodents. Developmental effects include exencephaly and spina bifida. Reproductive effects include reduced fertility and fewer and smaller litters (ATSDR, 1989).

GENOTOXICITY

There is a large database on the mutagenicity of DEHP involving a large number of tests conducted in bacterial systems as well as in in vivo and in vitro mammalian test systems. In addition, a less extensive database is available on the mutagenicity of the metabolites, MEHP and 2-ethylhexanol. The overall weight of evidence indicates that DEHP is not mutagenic (ATSDR, 1989). A carcinogenic feeding bioassay conducted by the National Toxicology Program (NTP) in B6C3F1 mice and F344 rats found an increased incidence of hepatocellular tumors which increased with increasing dose (NTP, 1982). EPA has designated DEHP as a B2, Probable Human Carcinogen.

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CADMIUM

GENERAL BACKGROUND INFORMATION

Cadmium typically exists in the environment as a salt of the +2 valence state or as a metal. It forms no stable organic compounds. Cadmium releases are generally associated with mining, smelting, manufacturing operations, and from the disposal of alkaline batteries containing cadmium (Doull, 1980; U.S. EPA, 1981).

PHARMACOKINETICS

Cadmium is absorbed by all routes of exposure (see section on Relative Absorption Factors). Absorption through the gastrointestinal tract is low, respiratory absorption more efficient and dermal absorption relatively insignificant (ATSDR, 1989). Absorbed cadmium is widely distributed throughout the body, with the major portion of the body burden located in liver and kidney (Sumino et al., 1975). The distribution of cadmium is linked to the distribution of metallothionein, a low-molecular-weight protein, rich in cadmium-binding sites. Cadmium is not known to undergo any direct metabolic conversions in vivo. The principle excretory route for absorbed cadmium is urinary. Excretion is slow, accounting for the long half-life of cadmium in the body (17-38 years) (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Cadmium is a local respiratory tract irritant. Systemic symptoms occur in a few hours after an acute exposure to cadmium dust or fumes. Upper respiratory tract irritation is followed by coughing, chest pain, sweating, and chills. These symptoms resemble nonspecific upper respiratory infection (Sittig, 1985). Within 24 hours severe pulmonary irritation may develop, with progressively increasing pain in the chest, dyspnea, pulmonary edema, cough, and generalized weakness. Chronic exposure to cadmium fumes may result in emphysema-like lung damage (Sittig, 1984). Renal dysfunction may ensue (Friberg, 1950). Bernard and Lauwerys (1984) observed that the gastrointestinal tract is adversely affected by acute oral exposure with such symptoms as nausea, vomiting, salivation, abdominal pain, cramps, and diarrhea. The principal effects of chronic cadmium exposure are osteomalacia and osteoporosis (Itai Itai disease) secondary to glomerular and tubular necrosis in the kidney. The Itai Itai ("ouch-ouch") disease is endemic areas in Japan, which have been contaminated with mining wastes containing cadmium. Victims display the osteomalacia and osteoporosis as primary symptoms, as well as protein, sugar and amino acids not normally found in the urine. Other chronic effects include immunosuppression and decreases in measures of respiratory fitness (ventilation capacity, vital capacity, forced expiratory volume, etc.) (U.S. EPA, 1981).

MAMMALIAN TOXICOLOGICAL PROFILE

Several subchronic and chronic oral toxicity studies have been conducted in animals. Koller et al. (1975) and Fitzhugh and Meiller (1941) conducted feeding studies using mice and rats, respectively. The first group of researchers reported immunological impact manifested by a decrease in the number of lymphocytes secreting antibodies (to sheep red blood cells) as well as some renal effects. The second set of authors observed hematological symptoms expressed as marked anemia. Yuhas et al. (1979) conducted a drinking water study using Sprague-Dawley male rats. Decreased weight gain was observed at the highest dose level. In addition, the authors identified increases in cadmium content and decreases in the zinc content of the bone. Renal dysfunction or otherwise generalized adverse effects on the kidney have been reported in a number of long-term cadmium ingestion studies (Friberg et al., 1974; Kijikawa et al., 1981; Schroeder et al., 1964; Kanisawa and Schroeder, 1969). In addition, the latter two research groups have observed renal and cardiac arteriosclerosis.

GENOTOXICITY

Results of mutagenicity tests in bacteria and yeasts have been inconclusive. Positive results have been obtained in mutation assays in Chinese hamster cells and in mouse lymphoma cells. Conflicting results have been obtained in assays of chromosomal aberrations in human lymphocytes treated in vitro or obtained from exposed workers. Cadmium treatment in vitro or in vivo appears to result in aneuploidy in germ cells of mice or hamsters (ATSDR, 1989). Reports of elevated prostate cancer in cadmium workers have been evaluated as insufficient evidence of the carcinogenic action of the compound (U.S. EPA, 1985), but the elevated risk of lung cancer observed by Thun et al. (1985) is more convincing. Thus, the carcinogenic potential of inhaled cadmium should be viewed as limited, but suggestive. Although ingestion of cadmium may result in kidney effects, no carcinogenic response has been demonstrated for this route.

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CARBON TETRACHLORIDE

GENERAL BACKGROUND INFORMATION

Carbon Tetrachloride is a clear, heavy aromatic liquid with a sweet odor. Although this compound does not occur naturally, it is distributed extensively in the earth's atmosphere due to its extensive anthropogenic production and use. Carbon tetrachloride is currently widely used as a refrigerant and a propellant. Carbon tetrachloride is also used a solvent for oil, fats, lacquers, varnishes, rubber, waxes and resins. Until the mid-1960s, carbon tetrachloride was used as an industrial degreaser, as a household spot remover, and as a fire-extinguishing agent. Until 1986, carbon tetrachloride was used to fumigate grain. Carbon tetrachloride is very stable in the atmosphere, with a half-life in air of about 30-100 years. Thus, it persists in the environment for many years (Sittig, 1981; ATSDR, 1989).

PHARMACOKINETICS

Carbon tetrachloride is readily absorbed through ingestion and inhalation and poorly absorbed through the skin (see section on Relative Absorption Factors). The metabolism of carbon tetrachloride occurs primarily in the liver, where a specific form of hepatic cytochrome P-450 initiates a reductive dehalogenation yielding a trichloromethyl free radical and a chloride ion. The trichloromethyl radical is then further reacted upon either anaerobically or aerobically. Anaerobically, either CHCl_3 , Cl_3CCCl_3 or $\text{CO}^+/\text{HCOO}^-$ can be produced depending on which of several anaerobic reactions take place. Aerobically, the precursor, Cl_3CO_2 could be produced, leading to formation of phosgene (COCl_2). Hydrolytic cleavage of COCl_2 leads to formation of HCl . Although it is known that metabolism of carbon tetrachloride plays an important role in its toxicity, the specific mechanism relating the metabolites to toxicity has not yet been determined. Excretion of carbon tetrachloride from the body has been found to occur largely in the form of the parent compound. Exposure studies in animals have shown that about 30-40% of an inhaled dose of carbon tetrachloride is recovered in expired air and about 50-60% is recovered in feces. Via oral exposure, one rat study indicated that about 70-90% of an administered oral dose was recovered in expired air and lower amounts were recovered as CO_2 or CHCl_3 or as nonvolatile metabolites in feces or urine. Via dermal exposure, carbon tetrachloride excretion has also been found to occur rapidly through expired air, but this was not quantified (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Most of the human health data for carbon tetrachloride come from acute exposure case studies in individuals who have been exposed to large doses for short periods of time. Health effects of carbon tetrachloride include defatting of skin leading to a dry, fissured dermatitis

and transient eye irritation. Acute exposure is associated with central nervous system depression, gastrointestinal effects, and liver and kidney damage. Specific symptoms include headache, dizziness, nausea, vomiting and in severe cases, stupor or coma, with the potential for permanent damage to nerve cells. Liver damage can be manifested with nausea, vomiting, abdominal pain, diarrhea, enlarged and tender liver, jaundice and fatty liver (symptoms of toxic hepatitis) (ATSDR, 1989; Sittig, 1989). Kidney damage can result in a more slowly accumulating, lower urinary volume, the presence of red and white blood cells in urine, albumuria, coma and death (Sittig, 1981). Kidney failure, resulting in the accumulation of waste products in the blood and accumulation of water in the body, especially the lungs, is a major cause of death from carbon tetrachloride. Effects to the liver and kidney are reversible after exposure ends, if damage is not too severe (ATSDR, 1989; Sittig, 1981).

MAMMALIAN TOXICOLOGICAL PROFILE

Acute oral toxicity in animals was found to occur at 4,000 mg/kg, producing respiratory edema, atelectasis and hemorrhage (Gould and Smuckler, 1971). The effects of carbon tetrachloride have been widely studied in animals. A range of adverse liver effects have been found including destruction of the endoplasmic reticulum and associated enzyme activities, inhibition of protein synthesis, impaired secretion of triglycerides with resultant fat accumulation and centrilobular necrosis (ATSDR, 1989). The kidney has also been found to be a target organ for carbon tetrachloride in animal studies, although in animals, carbon tetrachloride is more toxic to the liver than to the kidney (ATSDR, 1989). In animals administered oral doses of 1,400 mg/kg/day during gestation, maternal toxicity and total resorption of fetuses occurred in some animals but no teratogenic or other apparent effects were evident in offspring (Wilson, 1954). In rats exposed to carbon tetrachloride in food for five generations, no reproductive toxicity was noted of parameters investigated (% conception, % with litters, mean litter size, mean body weight of offspring at birth and at weaning). An increase in neonatal mortality was found in the low dose (6 mg/kg/day) group but not at the higher dose (15 mg/kg/day).

GENOTOXICITY

There is no available information on the mutagenic effects of carbon tetrachloride in humans. Very little information was found for carbon tetrachloride in animals. In one study in which rats were exposed orally to carbon tetrachloride, an increase in DNA synthesis associated with tissue regeneration was found, but no increase in unscheduled DNA synthesis. One study in yeast found suggestive evidence of mutagenicity but this test was conducted using concentrations of carbon tetrachloride significantly above the solubility of carbon tetrachloride in water (Callen, et al., 1980). EPA has designated carbon tetrachloride as a group B2 (Probable Human Carcinogen) based on conclusions by both EPA and the

International Agency for Research on Cancer (IARC) that sufficient evidence exists to designate this compound carcinogenic in experimental animals (ATSDR, 1989).

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CHLOROBENZENE

GENERAL BACKGROUND INFORMATION

Chlorobenzene is a clear liquid with an almond-like odor. Although chlorobenzene does not occur naturally in the environment, it is used in industry as a solvent, in the manufacture of aniline, phenol and chloronitrobenzene, and as an intermediate in the manufacture of dyestuffs and pesticides (ATSDR, 1990; Sittig, 1981).

PHARMACOKINETICS

Chlorobenzene is assumed to be readily absorbed via ingestion, moderately absorbed through inhalation and poorly absorbed through the skin, based on its structural similarity to benzene (see section on Relative Absorption Factors). The major metabolites of chlorobenzene are p-chlorophenylmercapturic acid and 4-chlorocatechol. Excretion of chlorobenzene occurs via urine in the form of its two metabolites, with the excretion of p-chlorophenylmercapturic acid reported to be much lower than of 4-chlorocatechol. A portion of an absorbed dose is excreted as unchanged chlorobenzene through the lungs (ATSDR, 1990).

HUMAN TOXICOLOGICAL PROFILE

Acute exposure to chlorobenzene has produced the following health effects in workers exposed to high levels: irritation of the eyes and nose, skin irritation, central nervous system depression with symptoms such as drowsiness, incoherence, numbness, nausea and vomiting. However, these workers were simultaneously exposed to other solvents so it is not clear whether chlorobenzene is responsible for these effects (ATSDR, 1990; Sittig, 1989).

MAMMALIAN TOXICOLOGICAL PROFILE

Acute lethality via both inhalation and ingestion is relatively low in animals. One study produced 100% mortality in mice after 2 hrs of exposure to 4,300 ppm. In rats exposed to a single dose of 4000 mg/kg and mice exposed to a single dose of 1000 mg/kg via corn oil by gavage, death occurred in 2-3 days (ATSDR, 1990). Animal studies indicate that exposure to chlorobenzene via either inhalation or ingestion can produce severe kidney and liver damage. Typical signs of liver damage reported include increased serum enzymes, changes in liver weights, degeneration, necrosis and interference with porphyrin metabolism. Signs of kidney damage include degeneration or focal necrosis of proximal tubules and increased kidney weights. Animal evidence also exists that chlorobenzene is immunotoxic via ingestion with the potential of producing thymic necrosis and lymphoid or myeloid depletion of bone marrow, spleen or thymus. Neurological effects, manifested by miscellaneous spasms and

narcosis, have been shown in animals acutely exposed via inhalation to chlorobenzene. There are very few animal data on the developmental and reproductive effects of chlorobenzene. The available data do not indicate that chlorobenzene produces developmental or reproductive effects via either inhalation or ingestion.

GENOTOXICITY

There were no data located regarding the mutagenicity of chlorobenzene in either animals or humans following oral exposure. Limited in vitro mutagenicity testing in bacterial and mammalian test systems suggest that chlorobenzene may not be genotoxic in humans (ATSDR, 1990). In a National Toxicology Program (NTP) chronic, oral carcinogenic bioassay conducted in both sexes of mice and rats, the only significant finding was an increase in the incidence of neoplastic nodules of the liver of male rats in the higher dose group but not at the lower dose. On the basis of these data, EPA has classified chlorobenzene as a Class D carcinogen (inadequate evidence of carcinogenicity in both humans and animals) (ATSDR, 1990; NTP, 1985).

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CHLOROFORM

GENERAL BACKGROUND INFORMATION

Chloroform is a clear, colorless, liquid with a characteristic odor, which exists both naturally and as a man-made compound. Chloroform was one of the earliest general anaesthetics but was later banned because of toxic effects. Chloroform is largely used in the production of fluorocarbon 22 (used as a coolant in air conditioners and to make fluoropolymers) (ATSDR, 1989). In addition, chloroform is used as a solvent, in the extraction and purification of pharmaceuticals, in the manufacture of pesticides and dyes and in various products including fire extinguishers, dry cleaning agents, artificial silk, plastics and floor polishes. Chloroform is also widely found in drinking water supplies as a byproduct of chlorination (ATSDR, 1989; Sittig, 1981).

PHARMACOKINETICS

Chloroform is readily absorbed via inhalation and ingestion and poorly absorbed through the skin, unless the dose is occluded, in which case it is very well absorbed (see section on Relative Absorption Factors). Chloroform is lipid-soluble and passes through cell membranes easily. Thus it will reach the central nervous system and cross the placental barrier. It has been found in fresh cow's milk and is thus expected to reach human milk too. Chloroform is metabolized via cytochrome P450 by oxidative dechlorination to form phosgene. The phosgene either reacts with glutathione to form diglutathionyl dithiocarbonate or causes cytotoxicity directly by reacting with other cellular constituents. Inorganic chloride ion and carbon monoxide are minor metabolites of chloroform metabolism. Although there are species differences as to relative amounts metabolized, chloroform is largely excreted unchanged through the lungs. Carbon dioxide is also a major endproduct of chloroform metabolism, most of which is excreted via the lungs but some of which is also incorporated into endogenous metabolites and excreted as bicarbonate, urea, methionine and other amino acids. Carbon monoxide is a minor metabolite also excreted through the lungs. In addition, inorganic chloride ions are excreted via the urine (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Skin contact with chloroform can produce burns. Chloroform is a central nervous system depressant and was used in the past as an anaesthetic until it was determined that it caused liver and kidney toxicity. Specific central nervous system symptoms resulting from acute exposure include fatigue, dizziness, headache, digestive disturbance and mental dullness, as well as

coma at high levels. Chronic exposure has produced liver and kidney enlargement and jaundice (Sittig, 1981; ATSDR, 1989).

MAMMALIAN TOXICOLOGICAL PROFILE

Chloroform is acutely toxic via inhalation, with an LC50 of 10,000 ppm for 4 hours in rats (Lundberg et al., 1986). A concentration of 1025 ppm for 1-3 hours was lethal to mice (Derringer et al., 1958). The lowest oral LD50 value reported for rats is 444 mg/kg (Kimura et al., 1971). In a 90 day study, rats exposed to chloroform via the oral route had an increased mortality at 350 mg/kg/day (Chu et al., 1982). Chloroform has been found to target the liver, kidney and central nervous system in animal studies, after inhalation or oral exposure. Central nervous system effects found in animals via inhalation exposure include disturbed equilibrium (cats) at 7,200 ppm, deep narcosis (mice) at 4,000 ppm and slight narcosis (mice) at 2,500 ppm. Liver effects found in lab animals include fatty infiltration, focal necrosis, lobular granular degeneration and increased enzyme levels (SGOT, SGPT). Kidney effects include cloudy swelling, increased weight, tubular necrosis and tubular regeneration. Developmental effects observed after inhalation exposure include increased incidence of missing ribs, imperforate anus, subcutaneous edema and delayed and abnormal ossifications. In a questionable study, pregnant rats treated during gestation via gavage with 126 mg/kg/day were found to produce fetuses with reduced body weight. Reproductive effects found in lab animals include a significant increase in percentage abnormal sperm and gonadal atrophy (ATSDR, 1989).

GENOTOXICITY

The genetic toxicology database for chloroform indicates mixed results in mutagenicity tests. Negative results were obtained in bacteria and gene mutations, as well as chromosome aberrations in mammalian cells. Mixed results were obtained in yeasts. In vivo test results include negative results in *Drosophila* and DNA damage in rats and mice, whereas tests for chromosome aberrations and sperm abnormalities were mixed. Although the available data on genotoxicity suggests that chloroform may be mutagenic, the overall evidence is currently inconclusive (ATSDR, 1989). Carcinogenicity data via the inhalation route are currently not available for chloroform. A number of animal studies have indicated that chloroform is carcinogenic by the oral route. A 1976 NCI gavage study found a dose-related increased incidence of hepatocellular carcinoma in mice (NCI, 1976). A number of studies have found an increased incidence in kidney tumors (Roe et al., 1979; Jorgensen et al., 1985). Based on the above data, the Environmental Protection Agency (EPA) has designated chloroform a B2 carcinogen.

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CHROMIUM

GENERAL BACKGROUND INFORMATION

Chromium is used in plating for corrosion resistance and decorative purposes (appliances, tools, automobiles, etc.), in the manufacture of alloys (including stainless steel and heat resistant alloys), and in printing, dyeing, photography, tanning, and numerous other industrial applications (ATSDR, 1989).

PHARMACOKINETICS

Absorption studies of chromium compounds indicate that it is absorbed by all routes of exposure (see section on Relative Absorption Factors) with chromium (VI) compounds being more readily absorbed than chromium (III) compounds. Once absorbed, chromium is rapidly distributed to all organs, including the developing fetus. Chromium VI is readily reduced to Cr III in vivo. Excretion occurs primarily through the kidneys via urine (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

In humans, the respiratory tract is the primary system of concern for chromium toxicity. Renal damage has also been observed. Hexavalent chromium has been shown to be highly toxic, causing ulceration of nasal mucosa and carcinoma of the lung following long-term occupational exposure. Cases of acute poisoning in man have been reported from the medical use of chromic acid.

Chronic exposures of workers in chromium-related industries have been observed to result in skin and nasopharyngeal irritations. Both Cr(III) and Cr(VI) can cause allergic contact dermatitis and irritation (Samitz and Shrager, 1966). Chromium was shown to be an allergen in recurrent contact dermatitis of the feet (Correia and Brandao, 1986). Hexavalent forms are responsible for effects on the upper respiratory system, including ulceration and perforation of the nasal septum, chronic rhinitis, and pharyngitis. Lindberg and Hedenstierna (1983) reported that subjective and objective evidence of adverse nasal effects were found at exposure levels of 2 to 20 ug Cr(VI)/m³ but not at less than 1 ug/m³. They also reported that workers exposed to 2 to 20 ug Cr(VI)/m³ had slight transient decreases in measures of pulmonary mechanics (e.g., forced vital capacity, FVC) with recovery (no changes) seen by two (non-exposed) days later.

MAMMALIAN TOXICOLOGICAL PROFILE

In laboratory animals, Cr compounds are of low oral acute toxicity. Hexavalent chromium is more acutely toxic than Cr(III), with kidney failure being the primary symptom. The LC₅₀

in rats for inhalation of sodium chromate(VI) was reported as 33 mg Cr/m³/4H, and the LD₅₀'s for oral and dermal exposures were given as 16.7 mg Cr/kg and 514 mg Cr/kg, respectively (Gad et al., 1986). Chromium was found to localize in the proximal renal tubules when intraperitoneal doses of potassium dichromate were administered to rats 5 times weekly for 8 months (Berry et al., 1978). Low level hexavalent chromium exposure increases respiratory defense mechanisms while they are inhibited by long-term, high level exposure (Glaser et al., 1985). Chromium salts have been shown to be teratogenic and embryotoxic in mice and hamsters following intravenous or intraperitoneal injection. However, these are unnatural routes of administration for assessing effects of environmental exposures, and further research is needed (U.S. EPA, 1984).

GENOTOXICITY

Both Cr(III) and Cr(VI) have been shown to interact with DNA in bacterial systems. Cr(III) is generally considered to be a relatively inactive genotoxic agent since it is unable to cross cell membranes. It was recently shown, however, to cause chromosomal aberrations in human lymphocytes (Friedman et al., 1987). Hexavalent chromium has consistently caused transformations and mutations in a wide variety of in vitro assays (Bianchi and Lewis, 1985). Chromosomal damage has been observed in lymphocytes cultured from workers exposed to chromium. The epidemiologic studies of respiratory cancer in chromate production workers provide the bulk of the evidence for chromium carcinogenicity. Studies of chromate production facilities in the United States, Great Britain, and Japan have all found an association between occupational exposure to chromium and lung cancer (U.S. EPA, 1984). Workers were exposed to both Cr(VI) and Cr(III), and it is unclear whether Cr(VI) alone is the etiologic agent or whether Cr(III) is implicated as well. The U.S. EPA (1984) concluded that in rats, only calcium chromate had consistently produced lung tumors by several routes of administration, and that other Cr(VI) compounds produced local sarcomas or lung tumors in rats at the site of administration (subcutaneous, intraperitoneal, intermuscular, intrabroncheal, and intratracheal). Trivalent chromium compounds have not been found to be carcinogenic by any route of administration, but these compounds have not been studied as extensively.

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CHRYSENE

GENERAL BACKGROUND INFORMATION

Chrysene is one of the polycyclic aromatic hydrocarbon (PAH) compounds which are formed during the combustion of organic material. Chrysene often exists in particulate form, adsorbing to existing particulate material in air. Human exposure can occur in the workplace (coal and asphalt production plants, cooking plants, smoke houses) or in the environment due to chrysene contamination of air, food, soil and water (ATSDR, 1990).

PHARMACOKINETICS

Chrysene can be absorbed by all routes of exposure (see section on Relative Absorption Factors). Its absorption is believed to be qualitatively similar to benzo[a]pyrene (ATSDR, 1990). Following absorption, chrysene distributes to all organs, reaching the highest concentration in tissues with large fat content (adipose tissue, mammary tissue, brain) (Modica et al., 1983). Chrysene undergoes metabolic biotransformation mediated by the mixed function oxidase enzyme system to form reactive intermediates hypothesized to be responsible for its toxicity. The major metabolites include trans-dihydrodiols, phenols, diol epoxides and triol epoxides (Thakker et al., 1985). The reactive metabolites are conjugated and excreted primarily in feces (Schlede et al., 1970).

HUMAN TOXICOLOGICAL PROFILE

There is no information available on threshold toxic effects of chrysene in humans. Since it is structurally similar to benzo[a]pyrene, it would be expected to produce effects similar to B[a]P following acute or chronic exposure (see Toxicity Profile on Benzo[a]pyrene).

MAMMALIAN TOXICOLOGICAL PROFILE

There is no information available on threshold toxic effects of chrysene in animals. Since it is structurally similar to benzo[a]pyrene, it would be expected to produce effects similar to B[a]P following acute or chronic exposure (see Toxicity Profile for Benzo[a]pyrene).

GENOTOXICITY

The genotoxicity of chrysene has been evaluated in in vivo and in vitro cytogenetic tests. Chrysene produced weak positive results in bacterial mutation assays, human epithelial mutation studies, cell transformation assays and in vivo cytogenetic studies (Waters et al., 1987). Metabolism of chrysene is essential to produce the observed positive responses. Chrysene is not genotoxic in all test systems, however, it is believed to be a weak mutagen (ATSDR, 1990). The carcinogenicity of chrysene has not been adequately studied. There are no reports directly correlating human chrysene exposure and tumor development. There is limited evidence that chrysene is a skin carcinogen in animals following long-term dermal application (Wynder and Hoffmann, 1959; Hecht et al., 1974).

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CYANIDE

GENERAL BACKGROUND INFORMATION

Both cyanide gases and salts are used in industrial processes. Minor uses of HCN include insecticides and rodenticides for fumigating enclosed spaces (e.g., grain storage area). Cyanide salts are used mainly in the electroplating and metal-finishing industries. Minor applications of the salts include the manufacture of dyes and pigments, as well as use as insecticides and rodenticides (ATSDR, 1989)

PHARMACOKINETICS

Cyanide is readily absorbed following inhalation and oral exposure (see section on Relative Absorption Factors). Human and animal studies indicate cyanide is rapidly distributed by the blood following exposure (ATSDR, 1989). Metabolism involves (1) the conversion of cyanide to thiocyanate, (2) conversion to 2-aminothiazoline-4-carboxylic acid, (3) incorporation into a 1-carbon metabolic pool or (4) combining with hydroxycobalamin to form cyanocobalamin (ATSDR, 1989). Cyanide metabolites are excreted primarily in urine with small amounts eliminated through the lungs (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

The fatal effects of exposure to high doses of cyanide over short periods of time are well known. Inhalation of 100 ppm HCN for 0.5 to 1 hour has been fatal to humans. Exposure to HCN vapors resulted in palpitations, shortness of breath, pain over the heart, vertigo, and involuntary eye movements (Carmelo, 1955), cyanosis, headache, altered EEG, and left-sided blindness (Sandberg, 1967). The cardiovascular effects are believed to be secondary to the CNS effects (ATSDR, 1989). HCN fumigators also exposed by inhalation and dermal contact developed palpitations, shortness of breath, pain over the heart, vertigo, and involuntary eye movements (Carmelo, 1955). The LD₅₀ in humans for ingestion exposure has been reported to be 1.5 mg/kg/day of CN-. A lower fatal dose in humans has been reported at 0.6 mg/kg/day CN- (ATSDR, 1989). Brief exposure to lower levels of cyanide has resulted in rapid, deep breathing, shortness of breath, convulsions, and loss of consciousness. Because cyanide is not sequestered in the body, these effects are reversible over time. However, longer-term exposure to these low levels has resulted in CNS, thyroid gland, and cardiovascular effects. Several occupational studies of workers exposed to HCN produced thyroid abnormalities. In a case-control study of electroplating workers exposed to 6.4 to 10.4 ppm HCN for 5 to 15 years, 56 percent of the exposed group had enlarged thyroid glands and significantly elevated hemoglobin levels and lymphocyte counts. It should be noted that these workers were also exposed to volatiles, there were varying exposure levels,

and unmatched controls (El Ghawabi et al., 1975). Workers in a silver-reclaiming factory exposed an average of 10.5 months to a TWA of 16.6 mg/m³ HCN developed headache, dizziness, and mild thyroid abnormalities (Blanc et al., 1985). No studies of developmental effects in humans resulting from inhalation of cyanide are available.

MAMMALIAN TOXICOLOGICAL PROFILE

When monkeys were exposed to 87 to 196 ppm HCN, severe disruptive changes in respiration and unconsciousness were noted (Purser et al., 1984). Tremors, convulsions, loss of equilibrium, dyspnea, nausea, exaggerated intestinal peristalsis, and diarrhea were noted in dogs exposed to 45 ppm HCN for varying durations (Valade, 1952). When rats were exposed to inhalation of HCN at low concentrations, cardiac enzyme changes resulted (O'Flaherty and Thomas, 1982). The previously cited Purser study of monkeys exposed to 87 to 196 ppm HCN from pyrolyzed polyacrylonitrile also found cardiovascular effects, including rapid induction of a semiconscious state and severe disruptive changes in respiration.

Male rats were fed 30 mg/kg/day cyanide for 11.5 months and developed vacuolization and myelin degeneration of the spinal cord (Philbrick et al., 1979). No CNS effects were reported by Howard and Hanzell (1955) for rats fed up to 10.8 mg/kg/day of CN-in HCN-fumigated feed for two years. Dogs fed 0.27 and 0.53 mg/kg/day cyanide in capsules for 16 weeks developed degenerative changes in the CNS ganglion cells, reduced ribonucleic acid (RNA) content, and inflammation (Hertting et al., 1960). Numerous studies of orally exposed pregnant animals have found maternal toxicities and developmental abnormalities in the offspring. Pregnant hamsters exposed to cyanide as D,L-amygdalin (a component of laetrile) exhibited maternal toxicity at 250 mg/kg and greater. Fetuses were examined at 15-days gestation, and dose-related abnormalities were observed in this group (Willhite, 1982). Female rats were fed a basal cassava diet containing 12 mg/kg HCN and a basal diet with 1.25 gm KCN per kg diet prior to mating, during gestation, and through lactation. The weanlings were subsequently fed these same diets. Those weanlings exposed to higher levels of cyanide in utero and during the post-weaning period had significantly decreased protein-efficiency ratios. Both the dams and weanlings fed the potassium cyanide enhanced diet had significantly increased serum thiocyanate levels (Tewe and Maner, 1981).

GENOTOXICITY

Cyanides have tested negative for mutagenicity and effects on DNA synthesis except for a study by Kushi et al. (1983) in which a marginally mutagenic response for HCN was reported. There are no data available indicating that cyanide has any carcinogenic effects (ATSDR, 1989).

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DIBENZO[a,h]ANTHRACENE

GENERAL BACKGROUND INFORMATION

Dibenzo[a,h]anthracene is a member of the polycyclic aromatic hydrocarbons (PAH). PAHs are a class of compounds which are non-polar and contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. The data regarding dibenzo[a,h]anthracene are very limited. As a PAH, it is found in tobacco smoke, food, and the emissions from industrial or natural burning.

PHARMACOKINETICS

Dibenzo[a,h]anthracene is metabolized similarly to benzo(a)pyrene (ATSDR, 1990). However, while the metabolic profiles of these two compounds (and other alternant PAHs) are qualitatively similar, there are differences in the levels and rates of formation of specific metabolites among tissues and cell preparations used. Sanders et al (1986) applied ¹⁴C - dibenzo[a,h]anthracene to the shaved backs of mice. After 24 hours, the majority of activity was recovered from the application site, with the remainder from body tissues and excreta. In comparison, benzo(a)pyrene similarly applied was found predominantly in the excreta and body tissues, with the remainder at the application site.

HUMAN TOXICOLOGICAL PROFILE

The database for the toxicological effects of dibenzo[a,h]anthracene on humans, separate from other PAHs, is limited. Toxic effects attributable to mixtures of PAHs include a variety of skin lesions and non-cancer lung diseases such as bronchitis (IARC, 1973).

MAMMALIAN TOXICOLOGICAL PROFILE

Dibenzo[a,h]anthracene has been shown to induce skin tumors in lab animals (i.e. it is a complete carcinogen) following dermal exposure (Wyndner and Hoffman, 1959; Van Duuren et al, 1967; and Lijinsky et al, 1965). Dibenzo[a,h]anthracene has also demonstrated tumor initiation activity (Slaga et al. 1980).

Carcinogenic PAHs as a group has immunosuppressive effects, with the degree of immunosuppression correlated with carcinogenic potency (ATSDR, 1990). Dibenzo[a,h]anthracene was also tested for developmental effects via parenteral routes and was found to produce fetolethal effects in rats (Wolfe and Bryan, 1939).

GENOTOXICITY

Dibenzo[a,h]anthracene is mutagenic (Barfknecht et al, 1982; Rocchi et al, 1980) and produces DNA damage (Martin et al, 1978) in cultured human cells. Test results in nonhuman systems were also positive (ATSDR, 1990).

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1,1-DICHLOROETHANE

GENERAL BACKGROUND INFORMATION

1,1-Dichloroethane (1,1-DCA) is a colorless, oily, lipophilic liquid which evaporates quickly at room temperature and has an ether-like odor. Its liquid and vapor forms ignite easily and may pose a fire hazard when handled improperly. It does not dissolve easily in water. 1,1-DCA is used primarily as an industrial solvent and as a dissolving agent for paint, varnish, finish removers and grease (ATSDR, 1990).

PHARMACOKINETICS

Little information exists quantitating the absorption of 1,1-DCA. However, based on its chemical and physical properties, it would be predicted to be readily absorbed via any route of exposure (ATSDR, 1990). Once absorbed, it should be readily distributed to bodily tissues, with highest concentrations achieved in tissues of greatest lipid content (Sato and Nakajima, 1987). A large percentage of an administered dose is exhaled unchanged (Mitoma et al., 1985). The remainder undergoes biotransformation mediated by the microsomal mixed function oxidase enzyme system to yield reactive acylchloride metabolite(s) which covalently bind to cellular macromolecules (Colacci et al., 1985). An alternative MFO-mediated pathway yields 2,2-dichloroethanol which undergoes subsequent oxidation to dichloroacetaldehyde and dichloroacetic acid (McCall et al., 1983). These metabolites are excreted through urine or further metabolized to CO₂ (Sato and Nakajima, 1987).

HUMAN TOXICOLOGICAL PROFILE

Relatively little information is available on the health effects of 1,1-dichloroethane in humans. It induces central nervous system depression and anesthesia upon inhalation. In fact, it was used as an inhalation anesthetic in the past. The use of 1,1-DCA as an inhalation anesthetic was discontinued when it was discovered that this compound induced cardiac arrhythmias in humans at anesthetic doses ((Reinhardt et al., 1971). No studies were located concerning threshold effects of exposure on any other organ system.

MAMMALIAN TOXICOLOGICAL PROFILE

Limited data indicate that 1,1-dichloroethane is less toxic than its isomer, 1,2-dichloroethane and most other chlorinated aliphatic solvents (Parker et al., 1979). Exposure of animals to 1,1-DCA results in central nervous system depression which may be fatal if exposure levels are high (Plaa and Larson, 1965). Nephrotoxicity has been observed in cats and mice

following subchronic exposure. One study (Schwetz et al., 1974) suggests that exposure in utero results in retarded fetal development.

GENOTOXICITY

Results from in vitro genotoxicity test are conflicting. 1,1-DCA tested negative in the Ames assay (Nohmi et al., 1985) and in yeast cells (Bronzetti et al., 1987). However, it did increase the transformation frequency in hamster embryo cells (Hatch et al., 1983). In vivo studies suggest that 1,1-DCA may be genotoxic since it was found to covalently bind to DNA (Colacci et al., 1985). This chemical has been classified as a possible human (C) carcinogen by EPA. This classification is based on conflicting chronic bioassay results in mice (NCI, 1977; Klaunig et al., 1986).

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1,2-DICHLOROETHANE

GENERAL BACKGROUND INFORMATION

1,2-Dichloroethane (1,2-DCA or ethylene dichloride) is a clear, colorless, volatile liquid with a pleasant odor. Approximately 80% of 1,2-dichloroethane is used to produce vinyl chloride. It is also used to produce vinylidene chloride, 1,1,1-trichloroethane, TCE, PCE, aziridines and ethylene diamines. Minor applications include various solvent functions, use as a fumigant for grains, upholstery and carpets and as a lead-scavenging agent in gasoline (IRP, 1985).

PHARMACOKINETICS

1,2-DCA is readily absorbed through the lungs following inhalation exposure in both humans and animals (ATSDR, 1989). Absorption from the gastrointestinal tract is rapid and complete. Excretion of unmetabolized 1,2-DCA is almost exclusively via the lungs. However, metabolism and excretion of metabolites by other routes is extensive and dose related. Tissue distribution of 1,2-DCA is consistent with its lipophilic nature. It crosses the blood-brain and placental barriers and distributes into breast milk (U.S. EPA, 1985).

HUMAN TOXICOLOGICAL PROFILE

Short-term ingestion or inhalation of 1,2-DCA results in symptoms of CNS depression, gastrointestinal upset and systemic injury to the liver, kidneys and lungs (Clayton and Clayton, 1981). Long term exposure of workers to 1,2-DCA in an occupational environment have been associated with loss of appetite, nausea, vomiting, epigastric pain, irritation of the mucous membrane, neurologic changes and liver and kidney impairment (IRP, 1985).

MAMMALIAN TOXICOLOGICAL PROFILE

Acute inhalation exposure of a number of animal species to 1,2-DCA resulted in death in rats and guinea pigs at 400 ppm and in mice, rabbits and dogs at 1500 ppm (Heppel et al., 1945, 1946; Spencer et al., 1951). Liver and kidney effects were noted, as well as associated adverse effects to the respiratory and cardiovascular systems. A 15 percent increase in fat accumulation and an increase in liver triglycerides were observed in rats fed 80 mg/kg/day in the diet for 5 to 7 weeks (Alumot et al., 1976). No changes in liver weight was reported at this dose level. No hepatic effects were noted in the same study at 30 mg/kg/day. No hepatotoxicity was noted in mice administered up to 189 mg/kg/day in drinking water for 90 days (Munson et al., 1982). Chronic exposure of rats to 25 mg/kg/day in food for two years did not result in abnormalities in liver function as measured by transaminases and

cholesterol values (Alumot et al., 1976). No dose-related reproductive effects were seen in mice fed 5-50 mg/kg/day in drinking water (Lane et al., 1982) or rats fed diets containing 12.5 or 25 mg/kg/day (Alumot et al., 1976). Intermittent exposure (7 hr/day) of female rats to 4.69 +/- 7 ppm of 1,2-DCA for 4 months prior to the mating period followed by inhalation exposure during pregnancy resulted in a statistically significant increase in embryo mortality (Vozavaya, 1977).

GENOTOXICITY

In-vivo exposure of mice to 1000 ppm of 1,2-DCA vapors for 4 hours or to a single nontoxic oral dose of 100 mg/kg resulted in irreversible DNA damage as revealed by single-stranded breaks in the hepatocytes of mice (Storer et al., 1984). 1,2-DCA has been found to be carcinogenic in rats and mice following oral gavage exposure (NCI, 1978). A dose of 47 mg/kg/day administered to rats produced tumors at locations remote from the site of administration. Statistically significant increases in multiple tumor types (malignant and nonmalignant) were noted in treated animals of both species. An increased incidence of fibromas of the subcutaneous tissue and hemangiosarcomas of the spleen, liver, pancreas and adrenal gland was observed in male rats exposed to 47 or 95 mg/kg/day. Male rats exposed to 95 mg/kg/day were observed to have an increase in squamous-cell carcinomas of the forestomach, and female rats at this dosage had increased adenocarcinomas and fibroadenomas of the mammary gland.

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1,1-DICHLOROETHYLENE

GENERAL BACKGROUND INFORMATION

1,1-Dichloroethylene (1,1-DCE or vinylidene chloride) is a synthetic chemical used to make certain plastic products and flame retardant fabrics. It is released into the environment primarily as a result of air and water emissions coming from factories where 1,1-DCE is manufactured, hazardous waste sites where 1,1-DCE has been improperly disposed of, or as a result of accidental spills. 1,1-DCE is also found as a breakdown product of other chemicals present in the environment. Although high percentages of 1,1-DCE in soil and water quickly escape to the air, small concentrations remain and undergo biodegradation into other compounds. Once in the air, the compound rapidly decomposes through a variety of processes. It is estimated that 1,1-DCE released into the atmosphere persists for only about two days (ATSDR, 1988).

PHARMACOKINETICS

1,1-DCE is rapidly absorbed by the oral and inhalation routes. In animal studies, it was found to accumulate preferentially in the kidney, liver, and lung. 1,1-DCE undergoes complex biotransformation processes and numerous metabolites have been identified. The initial metabolic step is possibly the formation of an unstable reactive epoxide intermediate. Metabolites are ultimately conjugated with glutathione and excreted in urine (ATSDR, 1988).

HUMAN TOXICOLOGICAL PROFILE

Humans exposed to high concentrations of 1,1-DCE (approximately 4,000 ppm) show central nervous system depression which sometimes progresses to convulsions, spasm, and unconsciousness (Tierney et al., 1979). Repeated exposure to 1,1-DCE causes hepatotoxicity. Preliminary clinical findings on workers exposed to 1,1-DCE for up to 6 years in a polymerization plant in New Jersey revealed a high incidence of hepatotoxicity (U.S. EPA, 1985).

MAMMALIAN TOXICOLOGICAL PROFILE

Signs of central nervous system toxicity are the predominant effects observed in animals acutely exposed to high concentrations of 1,1-DCE via the inhalation route. The toxic signs consist primarily of central nervous system depression, lacrimation, dyspnea, tremor, convulsions, and narcosis, finally resulting in death (Klimisch and Freisberg, 1979a,b; Zeller et al., 1979). Rodents acutely exposed to high levels of 1,1-DCE (500 - 15,000 ppm) via inhalation show irritation of the mucous membranes and pulmonary edema, congestion and

hyperemia (Zeller et al., 1979). Acute inhalation exposure to 1,1-DCE produces cardiovascular effects, such as contraction of the main vessels, dilation of the right side, and hyperemia (Klimisch and Freisberg, 1979; Zeller et al., 1979). The liver is a major target organ for 1,1-DCE toxicity. Four-hour inhalation exposure to 200-250 ppm of 1,1-DCE resulted in increased liver weight, hepatic enzyme induction and massive histologic injury (Jackson and Conolly, 1985; Jaeger, 1977). Glutathione appears to play an important role in reducing the toxic effects of 1,1-DCE. For example, fasted rats which have depleted glutathione levels, display much greater 1,1-DCE induced toxicity (Reynolds et al., 1980). Acute exposure to 1,1-DCE also results in renal damage, with the severity of the kidney lesions increasing with increasing dose and duration of exposure (Reitz et al., 1980).

Long-term inhalation exposure to 1,1-DCE is associated with adverse respiratory effects as evidenced by irritation of the upper respiratory tract. Nasal irritation was observed in rats exposed to 200 ppm for 4 weeks (Gage, 1970). Other pulmonary effects seen in rats, guinea pigs, and dogs exposed to similar concentrations of 1,1-DCE for 90 days include discoloration and morphologic changes in the lungs (Prendergast et al., 1967). Quast et al. (1986) reported hepatotoxic effects in rats exposed to 21 ppm 1,1-DCE 6 hours/day, 5 days/week for six months. Studies by Short et al. (1977) demonstrated that inhalation exposure of pregnant rats to 1,1-DCE produced a statistically significant increase in early embryo resorptions in rats at 57 and 449 ppm, and in mice exposed at 57 ppm. Maternal lethality was also increased. 1,1-DCE induced weak teratogenic effects in laboratory animals. Prenatal exposure caused tissue anomalies in rats and skeletal defects in rats, mice and rabbits.

GENOTOXICITY

1,1-DCE is mutagenic in a number of test systems. In in vitro test systems, 1,1-DCE required metabolic activation before demonstrating mutagenicity. 1,1-DCE was mutagenic in *Salmonella* after metabolic activation with an exogenous activation system derived from human liver samples (Jones and Hathway, 1978), showing that human liver is capable of activating 1,1-DCE into mutagenic metabolites. In in vivo mutagenicity studies, 1,1-DCE did not produce mutations (Anderson et al., 1977). Inhalation of 1,1-DCE was associated with low rates of DNA alkylation in the livers and kidneys of mice and rats (Reitz et al., 1980). Out of several carcinogenicity studies conducted with 1,1-DCE, only one inhalation study provides evidence of a positive carcinogenic effect (Maltoni et al., 1985). In this study, increases in renal adenocarcinomas were noted in male Swiss mice exposed by inhalation to 25 ppm 1,1-DCE.

Van Duuren et al., (1979) evaluated the carcinogenicity of 1,1-DCE in mice treated by dermal application and by subcutaneous injection. 1,1-DCE was inactive as a complete carcinogen when applied repeatedly for a lifetime to mouse skin, and did not induce sarcomas after subcutaneous injection. However, a dermal initiation-promotion study indicated 1,1-DCE was

active as a tumor-initiating agent (Van Duuren et al., 1979). U.S. EPA has classified 1,1-DCE as a Group C agent (possible human carcinogen) for which there is limited evidence of carcinogenicity in animals.

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1,2-DICHLOROETHYLENE

GENERAL BACKGROUND INFORMATION

There are two isomers of 1,2-dichloroethene (1,2-DCE), cis and trans. Neither of these isomers has developed wide industrial usage in the United States partly due to their flammability. The trans isomer is more widely used in industry than either the cis isomer or the 60:40 cis/trans mixture. It is used as either a low-temperature extraction solvent or as a direct solvent in materials such as dyes, perfume oils, waxes, resins and thermoplastics. It is also used as a chemical intermediate in the synthesis of polymers. 1,2-DCE is highly volatile, weakly adsorbed by soil and has no significant potential for bioaccumulation. It may volatilize from soil surfaces, but that portion not subject to volatilization is likely to be mobile in groundwater (IRP, 1985).

PHARMACOKINETICS

1,2-DCE is absorbed by all routes of exposure (see section on Relative Absorption Factors) (ATSDR, 1989). Distribution is expected to be rapid. Due to the lipophilic nature of 1,2-DCE, tissues of high lipid content would be expected to attain the highest levels. 1,2-DCE is metabolised via the mixed function oxidase enzyme system to chloroethylene epoxides which undergo rearrangement to dichloroacetaldehyde or chloroacetic acids (Henschler, 1977; Liebman and Ortiz, 1977). Excretion of 1,2-DCE and its metabolites has been largely uncharacterized (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

1,2-DCE was once used as a general inhalation anesthetic in humans (Proctor and Hughes, 1978). Exposure to the trans isomer at a level of 2000 ppm causes burning of the eyes, vertigo and nausea (Proctor and Hughes, 1978). Within the limited industrial usage, only one toxic effect in humans was reported - a fatality due to very high vapor inhalation in a small enclosure (Rosenthal-Deussen, 1931). 1,2-DCE causes eye and skin irritation upon contact (Grant, 1974). There are no reports of long-term human exposure to 1,2-DCE isomers.

MAMMALIAN TOXICOLOGICAL PROFILE

Toxicological data for 1,2-DCE are limited, since it is not widely used. The only available data are old, and the purity of the samples could not be verified. According to Smyth (1956), the cis isomer did not kill or anesthetize rats in 4 hours at 8000 ppm. At 16,000 ppm, rats became anesthetized in 8 minutes and died in 4 hours. Smyth also stated that he found the trans isomer to be twice as toxic as the cis isomer. A 6-hour LC_{50} value of 22,000 ppm was reported for mice exposed to the trans isomer (Mathies, 1970). Adverse lung effects were reported in rats receiving a single 8-hour exposure to 200 ppm of the trans isomer (Freundt, 1977). Dogs repeatedly exposed to dichloroethylene vapor developed superficial corneal clouding which was reversible within 24 to 48 hours (Grant, 1974). There are conflicting data about the chronic toxicity of 1,2-DCE. Torkelson reported no adverse effects in rats, rabbits, guinea pigs and dogs exposed to either 500 or 1000 ppm of 1,2-DCE 7 hours daily, 5 days per week for 6 months. The sample consisted of 60% cis- and 40% trans-1,2-DCE (ACGIH, 1980). Similarly, no effects were seen in rats dosed subcutaneously, percutaneously or by ingestion (ACGIH, 1980). In contrast, Freundt et al. (1977) reported marked effects in rats exposed 8 hours daily, 5 days per week for 16 weeks to vapor levels of 200 ppm of the trans isomer. Liver and lungs were affected and leukocyte counts were decreased. No data on reproductive toxicity are available on the 1,2-DCE isomers (IRP, 1985).

GENOTOXICITY

Both isomers of 1,2-DCE were tested in Salmonella with and without activation in vitro and in vivo host-mediated assays. Both isomers were toxic but did not induce any genetic effects (Bronzetti et al., 1982). No carcinogenicity data are available for either the cis- or trans-isomers of 1,2-DCE. Neither IARC nor the NTP have evaluated 1,2-DCE (IRP, 1985).

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ETHYLBENZENE

GENERAL BACKGROUND INFORMATION

Ethylbenzene is a colorless liquid that smells like gasoline. It is volatile and flammable. Ethylbenzene occurs naturally in coal tar and petroleum, and is also manufactured for commercial uses in paints, inks, and insecticides (ATSDR, 1990). The two major uses of ethylbenzene are in the plastic and rubber industry, where it is used in the synthesis of styrene (U.S. EPA, 1980). Gasoline contains about 2% (by weight) ethylbenzene (ATSDR, 1990). Ethylbenzene has a wide environmental distribution due to its widespread use.

PHARMACOKINETICS

Ethylbenzene has been shown to be readily absorbed via inhalation, ingestion, and dermal exposure in humans as well as in laboratory animals (see section on Relative Absorption Factors). Following exposure, ethylbenzene is distributed throughout the body, with the highest levels detected in the kidney, lung, adipose tissue, digestive tract, and liver (Chin et al., 1980). There appears to be quantitative differences in metabolism of the chemical in humans and laboratory animals. However, in all species, ethylbenzene undergoes a variety of microsomal-mediated side-chain hydroxylations to yield the major metabolites, mandelic acid and phenylglyoxylic acid (Engstrom et al., 1984). The oxidation products are conjugated followed by urinary excretion which appears to be complete within 2 days of exposure (ATSDR, 1990).

HUMAN TOXICOLOGICAL PROFILE

Humans exposed to low levels of ethylbenzene in air for short periods of time experience eye and throat irritation. Exposure to higher levels may cause more severe effects such as central nervous system depression, decreased movement and dizziness, and more severe mucous membrane irritation. No studies have reported death in humans following exposure to ethylbenzene. No information was located to indicate that ethylbenzene produces toxicity in other organ systems upon short-term or prolonged exposure (ATSDR, 1990).

MAMMALIAN TOXICOLOGICAL PROFILE

Animal studies indicate that the primary symptoms resulting from acute exposure to ethylbenzene are manifested as neurological and respiratory depression. Other studies suggest that the liver, kidney and hematopoietic system may also be targets of ethylbenzene toxicity (ATSDR, 1990). Studies indicate that ethylbenzene exposure of pregnant rats can produce fetotoxic effects at doses that also induce maternal toxicity (Andrew et al., 1981).

Additionally, oral administration resulted in blockage of the estrus cycle in female rats (Ungvary, 1986).

GENOTOXICITY

Results of in vitro genotoxicity test generally indicate that ethylbenzene is not mutagenic in the presence or absence of metabolic activation (ATSDR, 1990). In one in vivo study, there was no dose-dependent increase in the frequency of micronucleated polychromatic erythrocytes (Mohtashamipur et al., 1985). Ethylbenzene did cause a mutagenic effect in mouse lymphoma cells and has been shown to induce a marginal yet significant increase in SCE in human lymphocytes. Therefore, ethylbenzene may cause an increased potential for genotoxicity in humans (ATSDR, 1990). No association between increased cancer incidence in humans and exposure to ethylbenzene has been reported. In animal studies, the only chronic bioassay produced inconclusive results of the tumorigenicity of oral ethylbenzene (Maltoni et al., 1985). Ethylbenzene is classified as a Group D agent (not classified as to carcinogenicity) by the EPA.

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ETHYLENE DIBROMIDE

GENERAL BACKGROUND INFORMATION

Ethylene dibromide (also known as EDB or 1,2-dibromoethane) is a colorless liquid with a mild, sweet odor, high volatility, and high water solubility. EDB is relatively persistent in groundwater and soil, but breaks down easily in air. The chemical is mostly man-made, and has been used as a pesticide and gasoline additive. EPA stopped most of its pesticide uses in 1984. EDB is added to leaded gasoline to produce better fuel efficiency, but because use of leaded gasoline has fallen, less EDB is made for this use. EDB may also occur naturally in the ocean in very small amounts (ATSDR, 1991).

PHARMACOKINETICS

EDB is readily absorbed by all routes of exposure (see section on Relative Absorption Factors). It is rapidly absorbed in the bloodstream and distributed but retained to a limited extent mainly in the kidneys, liver, and stomach (ATSDR, 1991). EDB is metabolized to active forms capable of inducing toxic effects by either oxidation or conjugation processes (ATSDR, 1991). Oral administration of EDB to rats primarily results in mercapturic acid derivatives excreted in the urine (74% of administered dose). Unmetabolized EDB may be excreted in the lungs, and a small amount (3%) may be excreted in feces (Plotnick et al, 1979).

HUMAN TOXICOLOGICAL PROFILE

Clinical signs in humans related to acute toxic exposure to EDB are depression and collapse, indicative of neurologic effects, and erythema and necrosis of tissue at the point of contact (oral and pharyngeal ulcers for ingestion, skin blisters and sloughing for dermal exposure). Acute deaths following toxic doses are related to cardiopulmonary arrest or, if affected individuals survive for a period of time, to hepatic and renal failure. Except for spermicidal effects in men after occupational exposures, chronic effects of EDB exposure have not been demonstrated in humans (ATSDR, 1991).

MAMMALIAN TOXICOLOGICAL PROFILE

Animals exposed to acute toxic doses of EDB experience similar clinical signs as noted above. Animal studies have also identified adverse ocular effects such as irritation and corneal damage after exposure to high concentrations of EDB (NTP, 1982). Neurologic signs were not reported in animals exposed by various routes over intermediate and chronic durations.

Developmental effects have been observed at doses that produced maternal toxicity. Antispermatic effects have been documented in animal studies ATSDR, 1991).

GENOTOXICITY

EDB is a potent mutagen, producing a broad spectrum of mutations in various test systems. There is sufficient evidence to indicate that EDB presents potential genotoxic risks for humans. There are no reports of cancer in humans associated with occupational exposure to EDB. However, EDB has been shown to be a potent carcinogen in rats and mice, causing malignant and benign neoplasms in multiple organ systems when administered by oral, inhalation, or dermal routes (ATSDR, 1991). EPA has classified EDB in the Carcinogen Assessment Group's Group B2: the evidence for carcinogenicity is adequate in animals but inadequate in humans (U.S. EPA, 1987).

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FLUORANTHENE

GENERAL BACKGROUND INFORMATION

Fluoranthene is a member of the polyaromatic hydrocarbons (PAH). PAHs constitute a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. Fluoranthene has been detected in food, cigarette smoke, and smoke from industrial and natural burning.

PHARMACOKINETICS

No data were found regarding the pharmacokinetics of fluoranthene.

HUMAN TOXICOLOGICAL PROFILE

The database for the toxicological effects of fluoranthene on humans, separate from other PAHs, is limited. Toxic effects attributable to mixtures of PAHs include a variety of skin lesions and non-cancer lung diseases such as bronchitis (IARC, 1973).

MAMMALIAN TOXICOLOGICAL PROFILE

The database on the toxicity of fluoranthene is limited. A 13 week subchronic study where CD-1 mice were gavaged with up to 500 mg/kg-day of fluoranthene indicated nephropathy, increased liver weights, hematological alterations and clinical effects (EPA, 1988). A developmental study in which fluoranthene was administered once via intraperitoneal injection to pregnant mice reported only an increased rate of embryo resorption (Irvin and Martin, 1987).

Chronic dermal application of up to 1 percent fluoranthene to the backs of mice did not induce skin tumors following lifetime application (Hoffman et al, 1972; Horton and Christian, 1974; and Wydner and Hoffman, 1959a). Fluoranthene is not a complete carcinogen (ATSDR, 1990) and does not exhibit initiation activity (Hoffman et al, 1972).

GENOTOXICITY

There is some evidence that fluoranthene is genotoxic (ATSDR, 1990). Genotoxic effects have been reported in human cells with exogenous metabolic activation, but negative results were recorded without metabolic activation.

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FLUORENE

GENERAL BACKGROUND INFORMATION

Fluorene is a member of the polycyclic aromatic hydrocarbons (PAH). PAHs constitute a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. The data on fluorene are very limited. Low levels of (5 to 67 ug/kg) have been detected in smoked meats (U.S. EPA, 1982).

PHARMACOKINETICS

No data were found regarding the pharmacokinetics of fluorene.

HUMAN TOXICOLOGICAL PROFILE

The database for the toxicological effects of fluoranthene on humans, separate from other PAHs, is limited. Toxic effects attributable to mixtures of PAHs include a variety of skin lesions and non-cancer lung diseases such as bronchitis (IARC, 1973).

MAMMALIAN TOXICOLOGICAL PROFILE

Limited information is available on the threshold effects of fluorene. An EPA study (EPA,1989) indicated that CD-1 mice exposed by gavage to up to 500 mg/kg-day of fluorene showed hypoactivity as well as a decrease in red blood cell count and packed cell volume and hemoglobin. Increases in absolute and relative liver, spleen and kidney weights was also observed. Gershbein (1975) reported that partially hepatectomized rats fed a diet of 180 mg/kg-day of fluorene for 10 days showed a statistically significant increase in liver regeneration, which is indicative of the ability to induce a proliferative response.

Fluorene is not reported to be a complete skin carcinogen (ATSDR, 1990). It was inactive as a tumor initiator when an estimated total dose of 1.0 mg was applied prior to the application of tetradecanoyl phorbol acetate (LaVoie et al, 1980).

GENOTOXICITY

There is no evidence that fluorene is genotoxic, but genotoxicity has been studied only in a few in vitro assays (ATSDR, 1990).

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INDENO[1,2,3-cd]PYRENE

GENERAL BACKGROUND INFORMATION

Indeno[1,2,3-cd]pyrene is a member of the polycyclic aromatic hydrocarbons (PAH). PAHs constitute a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. Indeno[1,2,3-cd]pyrene is present in cigarette smoke (IARC, 1983) as well as emissions from industrial stacks.

PHARMACOKINETICS

No data were found regarding the pharmacokinetics of indeno[1,2,3-cd]pyrene. However, its metabolism should be similar to another non-alternant PAH, benzo(b)fluoranthene (ATSDR, 1990).

HUMAN TOXICOLOGICAL PROFILE

The database for the toxicological effects of indeno[1,2,3-cd]pyrene on humans, separate from other PAHs, is limited. Toxic effects attributable to mixtures of PAHs include a variety of skin lesions and non-cancer lung diseases such as bronchitis (IARC, 1973).

MAMMALIAN TOXICOLOGICAL PROFILE

Studies on laboratory animals have demonstrated that indeno[1,2,3-cd]pyrene can induce skin tumors (i.e. it is a complete carcinogen) following dermal exposure (ATSDR, 1990). It has tumor initiating activity, but is not as potent as benzo(b)fluoranthene (Rice et al, 1985).

Carcinogenic PAHs as a group are immunosuppressant, with the degree of suppression correlated with the degree of potency (ATSDR, 1990)

GENOTOXICITY

In test systems using non-human cells, indeno[1,2,3-cd]pyrene was found to be genotoxic (ATSDR, 1990).

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LEAD

GENERAL BACKGROUND INFORMATION

Lead is used extensively in the manufacture of storage batteries and was used in gasoline and paint. Lead is also a natural constituent of many soils, for which concentrations normally range from 10 to 30 mg lead per kilogram of soil (U.S. EPA, 1980).

PHARMACOKINETICS

Lead can be absorbed by the oral, inhalation or dermal exposure routes (see section on Relative Absorption Factors). Gastrointestinal absorption of lead varies considerably depending upon chemical form, dietary intake, and age (Forbes and Reina, 1974; Barltrop and Meek, 1975). The deposition and absorption of inhaled lead depends upon particle size, chemical form and the rate and depth of breathing (Randall et al., 1975; Nozaki, 1966; Chamberlain et al., 1975). Once absorbed, lead is distributed to the various organs of the body, with most distribution occurring into mineralized tissues (ATSDR, 1990). Placental transfer to the developing fetus is possible (Bellinger et al., 1987). Inorganic lead is not known to be biotransformed within the body. Absorbed lead is excreted via the urinary or fecal routes (ATSDR, 1990)

HUMAN TOXICOLOGICAL PROFILE

Cases of acute lead poisoning in humans are not common and have not been studied in experimental animals as thoroughly as chronic lead poisoning. Symptoms of acute lead poisoning from deliberate ingestion by humans may include vomiting, abdominal pain, hemolysis, liver damage, and reversible tubular necrosis (U.S. EPA, 1984). Subacute exposures in humans reportedly may produce a variety of neurological effects including dullness, restlessness, irritability, poor attention span, headaches, muscular tremor, hallucinations, and loss of memory. Nortier et al., (1980) report encephalopathy and renal damage to be the most serious complications of chronic toxicity in man and the hematopoietic system to be the most sensitive. For this reason, most data on the effects of lead exposure in humans are based upon blood lead levels. The effects of lead on the formation of hemoglobin and other hemoproteins, causing decreased levels, are reportedly detectable at lower levels of lead exposure than in any other organ system (Betts et al., 1973). Peripheral nerve dysfunction is observed in adults at levels of 30 to 50 $\mu\text{g}/\text{dL}$ -blood. Children's nervous systems are reported to be affected at levels of 15 $\mu\text{g}/\text{dL}$ -blood and higher (Benignus et al., 1981). In high doses, lead compounds may potentially cause abortions, premature delivery, and early membrane rupture (Rom, 1976).

MAMMALIAN TOXICOLOGICAL PROFILE

Acute oral lethal doses of lead in animals depend upon chemical form, but generally range from 500 to 30,000 mg/kg. Several reproduction studies on the effects of subchronic oral exposure to lead in rats have been conducted (Kimmel et al., 1976; Grant et al., 1980; Fowler et al., 1980). These studies report that lead acetate administered in drinking water at various concentrations caused depressed body weights at 50 and 250 mg-Pb/L water, histological changes in the kidneys of offspring, cytokaryomegaly of the tubular epithelial cells of the inner cortex at concentrations greater than or equal to 25 mg/L and postnatal developmental delays at 50 to 250 mg/L. Higher oral doses of lead may result in decreased fertility and fetotoxic effects in a variety of species (Hilderbrand et al., 1973). A reduction in the number of offspring of rats and mice exposed to 25 mg Pb/L drinking water with a chromium deficient diet was reported by Schroeder et al. (1970). Chronic oral exposure of female Long-Evans rats to lead (5 mg/PB/L-water) reportedly resulted in slight effects on tissue excitability, systolic blood pressure, and cardiac ATP concentrations (Kopp et al., 1980a,b).

GENOTOXICITY

Results of *in vitro* studies with human lymphocyte cultures using lead acetate were nearly equally positive and negative. Results of *in vivo* tests are also contradictory but suggest that lead may have an effect on chromosomes (sister chromatid exchange).

Results for gene mutations, DNA modification, and recombinations in various microorganisms using lead acetate, lead nitrate and lead chloride were consistently negative with or without metabolic activation. Lead chloride has been reported to inhibit both DNA and RNA synthesis. In *in vitro* mammalian test systems, lead acetate gave conflicting results.

No epidemiological data regarding the oral carcinogenic potential of lead could be located in the available literature. Chronic inhalation may result in a statistically significant increase in deaths due to tumors in the digestive organs and respiratory systems in lead smelter workers and battery plant workers (Kang et al., 1980). Several studies have reported tumor formation in experimental animals orally administered specific lead salts, not normally ingested by humans (Zawirska and Medras, 1972; Boyland et al., 1962; Ito, 1973). The carcinogenicity of inhaled lead in experimental animals could not be located in the available literature. The U.S. EPA has classified lead and lead compounds as Group B2 - Probable Human Carcinogens.

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MERCURY

GENERAL BACKGROUND INFORMATION

Mercury has been used in the past for medicinal purposes (Gosselin et al., 1984). There are a number of occupations associated with mercury exposure, particularly through inhalation. These include mining, smelting, chloralkali production, and the manufacture of mercury-containing products such as batteries, measuring devices (thermometers) and paints. Mercury has also been used agriculturally as a seed and cereal protectant and as a fungicide.

PHARMACOKINETICS

The pharmacokinetics and pharmacodynamics of mercury depend largely on its chemical form, organic, inorganic or elemental. Absorption efficiencies vary depending on route of exposure and chemical form (see section on Relative Absorption Factors). Distribution, metabolism and excretion depend largely on the lipid solubility, ionization state and molecular size of the specific chemical form (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Exposure to most forms of mercury is associated with a high degree of toxicity. Elemental (metallic) mercury causes behavioral effects and other nervous system damage. Inorganic mercury salts do not generally reach the brain, but will produce kidney damage. Divalent (mercuric) mercury is substantially more toxic in this regard than the monovalent (mercurous) form. Organic mercury compounds are also toxic. Symptoms of chronic mercury poisoning can be both neurological and psychological in nature as the central nervous system is the primary target organ. Hand and finger tremors, slurred or scanning speech patterns, and drunken, stupor-like (ataxic) gait are some motor-control impairments that have been observed in chronic mercurial toxicity. Visual disturbances may also occur, and the peripheral nervous system may be affected. A psychological syndrome known as erethism is known to occur. It is characterized by changes in behavior and personality including depression, fearfulness, restlessness, irritability, irascibility, timidity, indecision, and early embarrassment. Advanced cases may also experience memory loss, hallucination, and mental deterioration.

MAMMALIAN TOXICOLOGICAL PROFILE

In a study by Mitsumori et al. (1981), male and female mice were fed methyl mercury chloride in their diet for up to 78 weeks. Most of the high dose group died from neurotoxicity before the 26th week. Renal tumors developed in 13 of 16 males in the

intermediate dosage group by 53 weeks while only 1 male in the control group developed tumors. No renal tumors occurred in exposed or control females. Studies on rats have reported similar effects such as damage to kidneys and the peripheral nervous system (U.S. EPA, 1980). Mice treated with alkyl mercury phosphate were reported to have an increased frequency of offspring with cleft palates (Oharazawa, 1968) while mice treated with methylmercury had offspring with significantly lowered birth weights and possible neurological damage (Fujita, 1969). No adequate epidemiological studies exist on the teratogenic effects of methylmercury on humans (U.S. EPA, 1980).

GENOTOXICITY

Skerfving et al. (1974) reported a statistical relationship between chromosome breaks and concentrations of methyl mercury in the blood of Swedish subjects on fish diets. Concentrations were reported to be from 14-116 ng Hg/ml in the blood of exposed subjects and from 3-18 ng/ml in nonexposed subjects.

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METHYLENE CHLORIDE

GENERAL BACKGROUND INFORMATION

Methylene chloride (also known as DCM or dichloromethane) is a colorless volatile liquid, has a mild sweet odor, and evaporates very quickly. DCM is widely used as an industrial solvent and paint stripper. It is also a component in certain pesticide and aerosol products. DCM is used in photographic film manufacturing. It has a high lipid solubility and modest solubility in water (ATSDR, 1989).

PHARMACOKINETICS

DCM is absorbed by all routes of exposure (see section on Relative Absorption Factors). Once DCM enters the body, absorption is through body membranes into the systemic circulation. In vivo studies have demonstrated two metabolic pathways: 1) an oxidative pathway mediated by the P-450 mixed function oxidase system yielding CO and CO₂, and 2) a glutathione-dependent (GST) pathway that yields CO₂. The GST pathway shows no indication of saturation at inhaled concentrations of up to 10,000 ppm (ATSDR, 1989). DCM is primarily eliminated in expired air as parent compound and the major metabolites CO and CO₂. A small amount of absorbed DCM has been detected in urine and feces (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Levels of >500 ppm of DCM in air can irritate the eyes, nose, and throat. If DCM is topically applied, it may cause only mild skin irritation because it evaporates quickly. CNS effects include lethargy, irritability, nausea, lightheadedness, and headaches. Symptoms usually dissipate quickly after exposure ends. Smokers may experience CNS effects at lower levels of DCM than non-smokers since smoking increases the CO content in blood. Hepatotoxicity is not evident in epidemiological studies. Adverse renal effects such as congestion and tubular changes show that DCM may be contributory, but not significant. Individuals with pre-existing cardiac disease may be more susceptible to DCM levels mediated by CO via CO-Hb (carboxyhemoglobin), depending on the inhaled concentration of DCM (ATSDR, 1989).

MAMMALIAN TOXICOLOGICAL PROFILE

Methylene chloride may cause acute lethality when animals are administered large doses by any route of exposure (ATSDR, 1989). The liver and the central nervous system are the primary targets following DCM exposure. CNS effects include narcosis, reduced REM during sleep and other behavioral manifestations. Liver toxicity, evidenced as histomorphological

alterations and alterations in liver cytochromes, was noted in a NCA drinking water bioassay (NCA, 1982) in rats. Limited data show that high concentrations of DCM can cause upper respiratory tract irritation and produce cardiovascular, ocular and renal effects (ATSDR, 1989).

GENOTOXICITY

Methylene chloride reportedly produced a dose related increase in chromosomal aberrations in peripheral lymphocytes of animals. Chromosome damage occurred at all dose levels and the extent of damage was greater in the presence of metabolic activation (Thilagar, 1983). No evidence of abnormalities in bone marrow cells in rats was reported (Burek, 1980). DCM was not found to be mutagenic in bacteria and yeast. Given evidence of in vitro DNA binding studies, the U.S. EPA (1987) concluded that DCM may be a weak mutagen in mammalian systems. Results were generally negative in vivo. Overall, DCM is considered to be a weak mutagen in lower species (ATSDR, 1989). In the NTP (1986) bioassay, significant increases with dose were reported in the incidence of neoplastic mammary tumors in male and female rats and for lung and liver tumors. A U.S. EPA assessment of the data produced by a NCA (1983) study concluded that significant increases in the incidence of hepatocellular adenomas/carcinomas were associated with the ingestion by mice of DCM in drinking water (EPA, 1985a). The U.S. EPA has classified DCM as a Group B2 -- Probable Human Carcinogen (U.S. EPA, 1985b).

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METHYL ETHYL KETONE

GENERAL BACKGROUND INFORMATION

Methyl ethyl ketone (also known as MEK or 2-butanone) is a colorless liquid with an acetone-like odor, moderate water solubility and high volatility. The major uses of MEK are as a solvent for coatings, adhesives and printing inks, as a cleaning/degreasing agent and as a chemical intermediate in the production of synthetic leathers, transparent paper and aluminum foil. MEK is a highly flammable substance and may pose a fire hazard if handled improperly (ATSDR, 1990).

PHARMACOKINETICS

MEK is readily absorbed by all routes of exposure (see section on Relative Absorption Factors). It is readily soluble in blood and appears to distribute uniformly to all organs (Perbellini et al., 1984). MEK is metabolized by both oxidative and reductive pathways (DiVincenzo et al., 1976). It undergoes reduction to 2-butanol and oxidation to 3-hydroxy-2-butanone, which is further reduced to 2,3-butanediol. Small amounts of unmetabolized MEK can be excreted in urine or exhaled air. All metabolites are excreted in the urine as glucuronides or sulfate conjugates.

HUMAN TOXICOLOGICAL PROFILE

MEK can produce irritation to the eyes, respiratory tract and skin following high level exposure. Central nervous system effects have been reported, including headache, dizziness, nausea and fatigue (ATSDR, 1990). No studies were located regarding the possible consequences of exposure on the liver, kidney, reproductive organs or developing fetus. This ketone has been demonstrated to be very hazardous in combination with other solvents by potentiating the neurotoxicity of n-hexane, methyl-n-butyl ketone and ethyl-n-butyl ketone (Altenkirch et al., 1979).

MAMMALIAN TOXICOLOGICAL PROFILE

High level inhalation exposure to MEK results in upper respiratory tract and ocular irritation. Exposure to high level MEK by the inhalation or oral route resulted in liver congestion, increase liver weight and renal tubular necrosis (Patty, 1935; Cavender et al., 1983). Narcosis and incoordination, indicators of central nervous system effects, were also observed, with no signs of peripheral neuropathy. Inhalation exposure during gestation resulted in fetotoxic effects such as reduced fetal weight, skeletal variations and delayed

ossification (Deacon et al., 1981; Mast et al., 1989; Schwetz et al., 1974). No studies were located regarding the possible consequences of exposure on the reproductive systems.

GENOTOXICITY

No in vivo studies were located regarding the genotoxicity of MEK. Results of in vitro tests indicate that MEK is nongenotoxic following in vitro exposure (Thorpe, 1982; O'Donoghue et al., 1988).

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2-METHYLNAPHTHALENE

GENERAL BACKGROUND INFORMATION

2-Methylnaphthalene is a member of the polycyclic aromatic hydrocarbons (PAH). PAHs are a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. This compound is used in the synthesis of organic chemicals and pesticides. The database for toxicological information is very limited.

PHARMACOKINETICS

No data were found regarding the pharmacokinetics of 2-methylnaphthalene.

HUMAN TOXICOLOGICAL PROFILE

No data were found regarding the human toxicity of 2-methylnaphthalene.

MAMMALIAN TOXICOLOGICAL PROFILE

No data were found regarding the mammalian toxicology of 2-methylnaphthalene.

GENOTOXICITY

No data were found regarding the genotoxicity of 2-methylnaphthalene.

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Agency for Toxic Substances and Disease Registry (ATSDR) (1990) Toxicity profile for naphthalene and 2-methylnaphthalene. U.S. Public Health Service.

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METHYL TERT BUTYL ETHER

GENERAL BACKGROUND INFORMATION

Methyl tert butyl ether (MTBE) is an volatile organic ether with extensive water solubility and lipophilicity. It is used clinically in the nonsurgical treatment of gallstones (Hofmann, 1990), as an industrial solvent and as a gasoline oxygenated octane enhancer. At normal temperature and pressure, it exists as a clear liquid with a disagreeable odor. MTBE is highly flammable and may pose a fire hazard if improperly handled (U.S. EPA, 1987).

PHARMACOKINETICS

Due to its lipophilicity, MTBE is well absorbed by all routes of exposure. It is readily soluble in blood and rapidly distributes to all organ systems, including fetal tissue, with highest concentrations occurring in organs with high lipid content such as adipose tissue and brain (U.S. EPA, 1987). Most of an administered dose is excreted unchanged in expired air (Biodynamics, 1984). The remainder undergoes oxidative metabolism mediated by the P-450 mixed function oxidase enzyme system to yield either tertiary butanol or formaldehyde which are ultimately eliminated from the body as either exhaled CO₂ or formic acid in urine and feces (Brady et al., 1990; Savolainen et al., 1985).

HUMAN TOXICOLOGICAL PROFILE

The only information concerning the human toxicity of MTBE involves its use as a therapeutic agent to dissolve gallstones. The procedure entails catheterization of the gallbladder through the abdominal cavity and subsequent perfusion with MTBE until the stones are dissolved. More than 400 patients have been treated worldwide with a high degree of success and few complications reported (Hofmann, 1990). Nausea, vomiting, sedation, local pain and mild hemolysis are possible side effects. The only major complication induced by MTBE has been a case of reversible renal failure in a patient during treatment (Ponchon, 1988).

MAMMALIAN TOXICOLOGICAL PROFILE

MTBE is considered to have a relatively low order of acute toxicity, evident from reported LD₅₀ values of 2962-3866 mg/kg and LC₅₀ values of 33,427-39,461 ppm (U.S. EPA, 1987). MTBE, in air, produces local irritation of the upper respiratory tract and mucous membranes. By all routes of exposure, it produces central nervous system depression evidenced as sedation, slowed reflexes, tremors, incoordination and altered behavior. Mild changes in

hematological parameters, neurobehavioral indices and organ weights were evident upon prolonged exposure (API, 1985).

Inhalation teratology and reproduction studies have failed to show any treatment related effects (Biodynamics, 1984).

GENOTOXICITY

Limited in vivo and in vitro cytogenetic results are available. In vivo, clastogenic effects were not observed in rats following subchronic exposure to MTBE (Bushy Run, 1989). In vitro tests similarly failed to show any correlation between MTBE exposure and cytogenetic abnormalities. MTBE did yield a dose-related positive response when tested in the mouse lymphoma forward mutation assay in the presence of metabolic activation. Negative results were obtained in the absence of metabolic activation (ARCO, 1987). No information on the carcinogenicity of MTBE was located. However, structure-activity analysis predicts MTBE to be neither a genotoxicant nor a carcinogen (Rosenkranz and Klopman, 1991).

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NAPHTHALENE

GENERAL BACKGROUND INFORMATION

Naphthalene is a white solid substance at room temperature. It has a distinct odor of mothballs or tar. Humidity and sunshine cause evaporation into the air within a few hours. When placed in water or soil, bacteria will destroy naphthalene, or will render it airborne within a few hours (ATSDR, 1990). Tobacco smoke is known to release 3 ug of naphthalene per cigarette (U.S. EPA, 1982). The compound is used in the production of dyes, solvents, lubricants, motor fuels (U.S. EPA, 1980) and is a major component of many moth ball preparations.

PHARMACOKINETICS

Humans can absorb naphthalene by dermal, inhalation and oral routes (see section on Relative Absorption Factors). Metabolism occurs via the P450 mixed function oxidase enzyme system to yield multiple intermediates which are then conjugated. Key metabolites are responsible for each toxicity endpoint following intraperitoneal administration: 2-naphthoquinones --> hemolysis; 1,2-naphthoquinones --> cataracts; 3-GSH adducts --> pulmonary toxicity (Buckpitt et al., 1984). Excretion of metabolites occurs via urine and feces (ATSDR, 1990).

HUMAN TOXICOLOGICAL PROFILE

Adults and children exposed to airborne naphthalene experience vomiting, abdominal pain and anemia (ATSDR, 1990). Most of the data is for inhalation of naphthalene from mothballs. The primary site of toxicity is the erythrocyte resulting in hemolytic crisis (hemolytic anemia). Jaundice is seen upon dermal, inhalation, and oral exposures, as are kidney effects (ATSDR, 1990). Near-blindness resulted in male and female subjects with 5 gram ingestion (ATSDR, 1990).

MAMMALIAN TOXICOLOGY PROFILE

Oral doses in rats have hepatic effects. Dogs (1800 mg/kg) for 5 days of exposure showed signs of lethargy and ataxia, and decreased hemoglobin levels (ATSDR, 1990)

GENOTOXICITY

No studies of genotoxic effects in humans or laboratory animals were located. No human epidemiological evidence for cancer.

Inconclusive evidence for cancer in rats and mice were found (ATSDR, 1990).

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NICKEL

GENERAL BACKGROUND INFORMATION

Nickel in the ambient atmosphere typically exists as a constituent of suspended particulate matter (U.S. EPA, 1985). The greatest volume of nickel emitted into the atmosphere is the result of fossil fuel combustion. Other sources of nickel emissions are primary production, incinerators, metallurgy, chemical manufacturing, cement manufacturing, coke ovens, nickel recovery, asbestos mining/milling and cooling towers.

PHARMACOKINETICS

Studies of nickel absorption have shown that it is absorbed by all routes of exposure to varying degrees, primarily dependent on the chemical form (see section on Relative Absorption Factors). Absorbed nickel is bound to serum components and distributed to body organs, reaching highest concentrations in kidney and lung tissue (Whanger, 1973). Nickel is not known to be biotransformed. Excretion of absorbed nickel is primarily through urine, with minor excretory routes through hair and sweat (ATSDR, 1988).

HUMAN TOXICOLOGICAL PROFILE

Nickel carbonyl $\text{Ni}(\text{CO})_4$ is a particularly toxic form of nickel upon inhalation and causes chest pain, dry coughing, hyperpnea, cyanosis, occasional gastrointestinal symptoms, sweating, visual disturbances and severe weakness. This is often followed by pulmonary hemorrhage, edema and cellular derangement. Survivors may be left with pulmonary fibrosis. In the workplace, nickel dermatitis may result at high nickel concentrations. At lower concentrations some susceptible individuals develop eczema-like lesions. The threshold for these health effects is much greater than exposures which occur in the ambient environment. The major adverse effects of nickel in man are dermatitis, chemical pneumonitis, and lung and nasal cancers.

MAMMALIAN TOXICOLOGICAL PROFILE

Deaths occurred in rats and mice at concentrations greater than 3.3 and 1.7 mg/m^3 nickel, respectively, upon extended inhalation exposure to NiSO_4 (Dunnick et al., 1987). Mice exposed to Ni_3S_2 died due to necrotizing pneumonia at 7.3 mg/m^3 nickel (Benson et al., 1987). Prolonged exposure of hamsters to nickel oxide at 41.7 mg/m^3 resulted in decreased survival due to emphysema (Wehner et al., 1975). Oral LD_{50} s in rats vary depending upon the nickel-containing compound to which the rats were exposed. These range from 355 mg compound/kg (118 mg Ni/kg) for nickel acetate (Haro, 1968) to greater than 5000 mg

compound/kg for nickel oxide, nickel sulfide, and nickel subsulfide (Mastromatteo, 1986). Rats fed diets containing nickel sulfate hexahydrate at 0, 250, 500 and 1000 ppm nickel showed no adverse effects over three generations in fertility, gestation, viability or lactation.

GENOTOXICITY

Weak evidence exists for the mutagenicity of nickel in bacterial and mammalian cells. Nickel appears to induce chromosomal aberrations in cultured mammalian cells (Larramendy et al., 1981), but not in vivo (Waksvik and Boysen, 1982). Occupational studies of human exposure indicate that certain nickel compounds appear to be carcinogenic via inhalation. However, there is no evidence of carcinogenicity in mammals through ingestion or dermal exposure (U.S. EPA, 1985). Nickel subsulfide has been found to be carcinogenic via the inhalation route in rats (Ottolenghi et al., 1974). Studies on nickel exposure via the oral route are inadequate to reach conclusions on carcinogenicity (ATSDR, 1988).

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PHENANTHRENE

GENERAL BACKGROUND INFORMATION

Phenanthrene is a member of the polycyclic aromatic hydrocarbons (PAH). PAHs constitute a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. The database on the potential health effects of phenanthrene is limited.

PHARMACOKINETICS

Little data are available regarding the pharmacokinetics of phenanthrene. The intestinal absorption of phenanthrene is less dependent on the presence of bile in the stomach than is the absorption of the larger PAHs (such as benzo(a)pyrene) (Rahman et al, 1986).

HUMAN TOXICOLOGICAL PROFILE

Phenanthrene has been shown to be a skin photosensitizer in humans (Sax, 1984).

MAMMALIAN TOXICOLOGICAL PROFILE

Phenanthrene has a reported LD 50 of 700 mg/kg in mice (Simmon et al., 1979). Rats injected intraperitoneally evidenced liver effects (Yoshikawa et al, 1987).

There is equivocal evidence for cancer from dermal application of phenanthrene in rats (IARC, 1983). Phenanthrene is not a complete skin carcinogen (ATSDR, 1990). It is neither an initiator (LaVoie et al, 1981; Roe, 1962) nor a promoter (Roe and Grant, 1964). Higgins and Yang (1962) reported no tumor production within two months after the ingestion of 200 mg of phenanthrene by rats.

GENOTOXICITY

There are limited data that suggest that phenanthrene is mutagenic (Wood et al., 1979). However, the majority of tests are negative (ATSDR, 1990).

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PHENOL

GENERAL BACKGROUND INFORMATION

Phenol is a colorless to white solid when pure, but the commercial product is a liquid. It has a sickeningly sweet and acrid odor, moderate solubility in water, low volatility, and has flammable characteristics. Phenol is mainly a man-made chemical, although it is found in nature in animal wastes and decomposing organic material (ATSDR, 1989). It is used in the production of a large variety of aromatic compounds, including explosives, fertilizers, coke, illuminating gas, lampblack, paints, paint removers, rubber, wood preservatives, synthetic resins, textiles, drugs, disinfectants, perfumes, and plastic. It is also used in the petroleum, leather, paper, soap, toy, tanning, dye, and agricultural industries (Clayton and Clayton, 1981).

PHARMACOKINETICS

Phenol is readily and rapidly absorbed by all routes and can produce symptoms within minutes of exposure to acutely toxic doses. In animals, phenol is rapidly distributed to the liver, heart, kidneys, lungs, blood, and muscle (ATSDR, 1989). Phenol then becomes fairly uniformly distributed before it is metabolized and excreted (U.S. EPA, 1980). After exposure, most of phenol is oxidized and conjugated with sulfuric, glucuronic, and other acids. It is excreted in the urine as "free" and as "conjugated" phenol. Only traces of "free" phenol are eliminated with the feces and expired air (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Acute poisoning by all routes of exposure may affect the central nervous system, leading to sudden collapse and unconsciousness. It may be lethal within minutes in humans due to respiratory failure. Swallowing phenol causes intense burning of the mouth and throat and abdominal pain (Clayton and Clayton, 1981). Ingestion of phenol in drinking water (daily doses of 10-240 mg) caused symptoms of diarrhea, mouth sores, and burning mouth (Baker et al., 1978). Repeated exposures to phenol at high concentrations have resulted in chronic liver damage (Merliss, 1972).

MAMMALIAN TOXICOLOGICAL PROFILE

The signs and/or symptoms of acute toxicity in humans and experimental animals are similar. The central nervous system effects observed in humans exposed to acute toxic doses are preceded in some animals by muscular twitchings and severe convulsions. In a severe

intoxication, there may be damage to the lungs, myocardial degeneration and necrosis, and liver damage (ATSDR, 1989).

GENOTOXICITY

No studies were located regarding genotoxic or carcinogenic effects in humans. The existing information on the mutagenicity of phenol is equivocal and needs to be re-examined to determine the mutagenicity of phenol. Cancer studies are inconclusive in animals (ATSDR, 1989). Phenol may have tumor promoting activity in certain strains of mice when repeatedly applied to shaved skin after initiation with known carcinogens (U.S. EPA, 1980).

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POLYCHLORINATED BIPHENYLS (PCBs)

GENERAL BACKGROUND INFORMATION

The thermal stability, nonflammability, and dielectric capability of PCBs resulted in their use in electrical capacitors and transformers (NIOSH, 1986). The manufacturing, processing, distribution in commerce, and use of PCBs after January 1, 1978 was prohibited under Section 6(e) of the Toxic Substances Control Act. PCBs can be released to the environment during fires involving electrical equipment containing these compounds. PCBs are strongly adsorbed on solid surfaces, including glass and metal surfaces in laboratory apparatus, and onto soils, sediments, and particulates in the environment.

PHARMACOKINETICS

Gastrointestinal absorption of most PCB isomers is large. PCBs can also be absorbed by the inhalation and dermal routes but limited data are available (see section on Relative Absorption Factors). Distribution of PCBs follows a biphasic pattern. Initially, PCBs distribute to liver and muscle tissue. They are then redistributed to the fat, skin, and other fat-containing organs (ATSDR, 1989). PCBs are poorly metabolized in humans with major metabolites being 3- or 4-hydroxy compounds. Metabolism may proceed through formation of arene oxide intermediates (U.S. EPA, 1988). The slow metabolism of PCB congeners to more polar compounds is responsible for long biological half-lives of PCBs. Excretion occurs primarily through the feces (Goto et al., 1974).

HUMAN TOXICOLOGICAL PROFILE

Dermatologic signs are the most persistent indicator of PCB toxicity. Skin manifestations have been observed also in newborn infants of mothers exposed to high levels of PCBs and related compounds. Cases of severe chloracne were reported in a work environment in which PCB air levels were found to be between 5.2 and 6.8 mg/m³. The workers developing chloracne had been exposed for 2 to 4 years. Other analyses revealed worker complaints of dry sore throat, skin rash, gastrointestinal disturbances, eye irritation, and headache at work area concentrations of 0.013 to 0.15 mg PCB/m³. Higher blood PCB levels are associated with higher serum triglyceride and/or cholesterol levels, as well as high blood pressure. Air PCB concentrations as low as 0.1 mg/m³ can produce toxic effects, and exposure to levels producing no overt toxicity can affect liver function. Recovery after termination of exposure occurs but is slow and depends upon the amount of PCBs stored in adipose tissue (Clayton and Clayton, 1981). Human exposures to PCBs resulting in toxic effects have almost all resulted from the ingestion of rice oil contaminated with "Kanechlor 400" in Japan (resulting in Yusho or rice oil disease) or from industrial exposure. Clinical symptoms of poisoning

included acne-like skin eruptions (chloracne), eyelid edema, conjunctival discharge, skin and nail pigmentation, and hyperkeratosis. Yusho patients are estimated to have ingested approximately 0.07 mg/kg/day for at least 50 days. The rice oil was found to be contaminated with polychlorinated dibenzofuran, which is believed to have played a significant role in the observed toxicity (Bandiera et al., 1984; Kashimoto et al., 1981). As suggested by laboratory experiments with Rhesus monkeys, fetal and newborn primates, including humans, may be particularly susceptible to PCBs. Fein et al. (1984) studied the effects of low-level chronic exposure to PCBs in pregnant women and their newborn offspring from consumption of Lake Michigan fish. Low levels of PCBs were reported to cause decreases in birth weight, head circumference, and gestational age of the newborn. PCBs were apparently transmitted to the fetus across the placenta and to the newborn through breast milk. Behavioral deficiencies, including immaturity of reflexes and depressed responsiveness, were reportedly observed in infants exposed to PCBs. Jacobson et al. (1984) correlated maternal consumption of PCB-contaminated fish with behavioral abnormalities in newborns, including autonomic immaturity and depressed responsiveness. The authors likened these responses to similar effects in laboratory animals.

MAMMALIAN TOXICOLOGICAL PROFILE

PCBs are only slightly toxic in acute exposures to laboratory animals. LD₅₀ values for rats, rabbits, and mice are generally in the range of 1 to 10 g/kg body weight (U.S. EPA, 1980).

Nonhuman primates seem to be particularly sensitive to PCB-induced reproductive effects (U.S. EPA, 1980). Dietary exposures of cynomolgus and Rhesus monkeys to 200 ug of Aroclor 1254/kg-day, 5 days per week for 28 months, resulted in symptoms of enlarged tarsal glands, conjunctivitis, loss of eyelashes, progressive detachment of fingernails, exuberant nail beds, hyperplasia of biliary ducts, hepatocellular enlargement and necrosis, and normocytic anemia (Tryphonos et al., 1986a; Tryphonos et al., 1986b). Effects were less pronounced in cynomolgus monkeys.

Monkeys that were fed diets containing 1.0 ppm of Aroclor 1016 for approximately 7 months prior to mating and during pregnancy delivered infants with reduced birth weights (Barsotti and Van Miller, 1984). Fetal mortality occurred at >2.5 ppm (0.1 mg/kg/day) of Aroclor 1248 in the diet in other studies with monkeys (Allen and Barsotti, 1976; Barsotti et al., 1976; Allen et al., 1980). In rats, a dose of 269 ppm of Aroclor 1254 given continuously in the food over the duration of pregnancy caused a decrease in the number of impregnated rats that delivered litters. Pups that were born were underweight, and most died within 7 days of birth. Two lower doses (26 and 2.5 ppm) caused altered neurobehavioral and somatic ontogeny (Overmann et al., 1987). PCBs have been shown to be teratogenic in mice. Cleft palate, dilated kidney pelvis, and thymus hypoplasia were observed. The ED50 (effective dose for 50% of the animals) for formation of cleft palate was a single 100 mg/kg dose, with peak sensitivity occurring on the twelfth day of gestation (d'Argy et al., 1987).

Immunological effects (decreased IgM, IgG induction) were noted in monkeys following a 27 month exposure at a dose of 0.005 mg/kg/day (Tryphonos et al., 1989).

GENOTOXICITY

Most genotoxicity assays of PCBs have been negative. The majority of microbial assays of PCB mixtures and various congeners show no evidence of mutagenic effects (U.S. EPA, 1980). The carcinogenic effects of PCBs have been studied in rats and mice. In a study conducted by Kimbrough et al. (1975) rats were exposed via the diet to 100 ppm Aroclor 1260 for 21 months. Hepatocellular carcinomas were observed in 26 of the 184 treated rats but only in one of the 173 controls. Neoplastic nodules were not found in controls but occurred in 144/184 of treated rats. The National Cancer Institute (NCI, 1978) reported a high incidence of hepatocellular proliferative lesions in male and female Fischer 344 rats fed three dose levels of Aroclor 1254 for 104-105 weeks, but, in part due to the small number of animals tested, carcinogenicity was not statistically demonstrable. Norback and Weltman (1985) fed a diet containing relatively high concentrations Aroclor 1260 (100 ppm for 16 months followed by 50 ppm for an additional 8 months) to Sprague-Dawley rats. In the PCB-exposed group, neoplastic nodules were observed at 12 months followed by trabecular carcinoma at 15 months and adenocarcinoma at 24 months (52/93). In the control rats, the incidence of hepatocellular neoplasms was low (1/81). Metastases to distant organs was not observed and mortality in the PCB exposed animals was not increased. The incidence of these slow-growing hepatocellular neoplasms was strikingly higher in female rats than in male rats.

PCBs (Clophen C) have also been shown to be cocarcinogenic. When PCBs were mixed with diethylnitrosamine (DNA), twice as many tumors were observed as were observed in animals treated with DNA alone (Brunn, 1987).

Based on the positive evidence for carcinogenicity of Aroclor 1254, Aroclor 1260, Kaneclor 500, and Clophen A-30 and A-60 in animals, along with adequate evidence in humans, the U.S. EPA has placed these PCBs in category B2 - probable human carcinogen (U.S. EPA, 1988).

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PYRENE

GENERAL BACKGROUND INFORMATION

Pyrene is a member of the polycyclic aromatic hydrocarbons (PAH). PAHs constitute a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. As with many of the other PAHs, pyrene has been detected in charbroiled meats and shellfish (U.S. EPA, 1982). It is found in tobacco smoke, industrial stack smoke, and smoke from forest fires.

PHARMACOKINETICS

No data were found regarding the pharmacokinetics of pyrene.

HUMAN TOXICOLOGICAL PROFILE

Pyrene is reported to be a skin irritant (Sax, 1984).

MAMMALIAN TOXICOLOGICAL PROFILE

Rats given 150 mg/kg of pyrene had changes in blood chemistry, liver and kidney damage (USEPA, 1982). A 1989 EPA study (EPA, 1989) reported nephropathy and decreased kidney weights in mice exposed to 125 mg/kg-day of pyrene by gavage for 13 weeks.

Mouse skin painting assays indicate that pyrene is neither a complete skin carcinogen, nor an initiating agent (ATSDR, 1990, IRIS, 1991).

GENOTOXICITY

The majority of genotoxic tests of pyrene are negative.

Positive results have been recorded in *Salmonella typhimurium* mutagenicity tests and in in vitro mammalian cell systems (ATSDR, 1990).

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SILVER

GENERAL BACKGROUND INFORMATION

Silver is used in photographic materials, batteries, paints and jewelry. Silver is used medically in dental amalgam and in medical supplies for burn treatment. Photographic materials are the major source of silver that is released into the environment. Trace amounts of silver are found in water from natural sources and industrial waste.

PHARMACOKINETICS

Studies in humans and animals indicate that silver compounds are absorbed readily by the inhalation and oral routes. Individuals and individual organs absorb silver selectively. The greatest concentrations are found in the reticuloendothelial organs. Silver undergoes oxidation and reduction reactions within the body and is excreted primarily via the fecal route (ATSDR, 1990).

HUMAN TOXICOLOGICAL PROFILE

Blue-gray discoloration of the skin has been observed in many individuals who have ingested metallic silver and silver compounds over periods of months to years. This condition is termed argyria. The pigmentation of the skin is primarily in sun-exposed areas. Silver-containing granules are also observed in the dermis. Gradual accumulation of 1 to 5 grams of silver will lead to generalized argyria. The discoloration is not known to be diagnostic of any other toxic effect (ATSDR, 1990). Occupational exposure to silver dusts can lead to respiratory and gastrointestinal irritation. The average air level was estimated to range from 0.039 to 0.378 mg/m³. Duration of employment ranged from less than one year to greater than ten years. Symptoms included abdominal pain, sneezing, stuffiness, and sore throat. Granular deposits were also observed in the conjunctiva and corneas of the eyes (Rosenman et al., 1979; 1987). Medical case histories indicate that dermal exposure to silver and silver compounds for extended periods of time can lead to local skin discoloration similar in nature to the generalized pigmentation seen after repeated oral exposure. The amount of silver and the duration of exposure necessary to produce this effect have not been established (McMahon and Bergfeld, 1983).

MAMMALIAN TOXICOLOGICAL PROFILE

Oral doses of 1,680 mg/kg silver colloid resulted in the deaths of rats after four days (Dequidt et al., 1974). Ingestion of silver nitrate and silver chloride will also cause deposition of silver granules in the skin of animals (Walker, 1971). Granules were observed in the eyes

of rats exposed to silver nitrate in drinking water at doses of 222 mg/kg/day over 37 weeks. These doses also cause general deposition in other tissues (Matuk et al., 1981). Mice given oral doses of 18.1 mg/kg/day silver nitrate for 125 days were observed to have silver deposits in their nervous systems. These animals were less active than unexposed controls (Rungby and Danscher, 1984). Silver has been found in the brains of neonatal rats whose mothers received silver lactate on days 18 and 19 of gestation (Rungby and Danscher, 1984). No studies were located that examine the reproductive effects of silver in animals or humans.

GENOTOXICITY

Silver is not mutagenic in bacteria but it has been found to cause DNA damage in mammalian cell culture (Robinson et al., 1982). No studies were located regarding cancer in humans or animals following oral, inhalation or dermal exposure to silver or silver compounds (ATSDR, 1990).

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TETRACHLOROETHYLENE

GENERAL BACKGROUND INFORMATION

The major use for tetrachloroethylene (perchloroethylene, PCE) is in the dry-cleaning industry. Its popularity in this area is due to its nonflammability, ease of recovery for reuse and its compatibility with various fabrics. It is also used in cold cleaning and vapor degreasing of metals. Its remaining uses are as a chemical intermediate in the synthesis of fluorocarbons, various manufacturing and industrial processes as well as medicinal uses (IRP, 1985).

PHARMACOKINETICS

PCE is readily absorbed by humans through the lungs into the blood. Pulmonary uptake is proportional to ventilation rate, duration of exposure and (at lower concentrations of PCE) to the concentration of PCE in the inspired air (Hake and Stewart, 1977). PCE is also rapidly absorbed following oral administration, but is poorly absorbed following dermal exposure (see section on Relative Absorption Factors). Distribution occurs rapidly with the highest concentrations of PCE achieved in tissues of high fat content (ATSDR, 1990). Metabolism of PCE is believed to be mediated by the microsomal mixed function oxidase enzyme system involving the formation of an epoxide intermediate. Major metabolites of PCE are trichloroacetic acid and trichloroethanol. Unmetabolized PCE is excreted largely by exhalation with urinary excretion of metabolites representing a small percentage (ATSDR, 1990).

HUMAN TOXICOLOGICAL PROFILE

Stewart et al. (1977) found that exposure of 11 subjects to a mean PCE concentration of 101 ppm for 7 hours produced symptoms of headache, dizziness, difficulty in speaking, and sleepiness. Long-term exposed subjects are also reported to experience effects such as short-term memory defects, ataxia, irritability, disorientation, and sleep disturbances (USEPA, 1985). PCE causes hepatotoxicity in humans. A number of reports of liver damage after inhalation of PCE in acute or chronic exposure situations have been documented (Hake and Stewart, 1977). PCE ingestion in humans results in symptoms indicative of liver damage, including elevated SGOT and SGPT levels, hepatomegaly, and fatty degeneration of the liver cells (Koppel et al., 1985).

MAMMALIAN TOXICOLOGICAL PROFILE

Male and female rats treated via stomach tube showed symptoms of tremors, ataxia, CNS depression, and finally, death (Hayes et al., 1986). Moderate fatty degeneration of the liver was observed in mice 1 day after a single 4-hour exposure to 200 ppm PCE, but not 3 days after exposure (Kylin et al., 1963). Chronic exposure in animals has been found to damage the CNS, producing symptoms such as hypertrophy and proliferation of astroglial cells in the brain (Rosengren et al., 1986). In this study, there was a decreased DNA content observed in the brain of gerbils exposed continuously to PCE concentrations as low as 60 ppm. It was suggested that this may represent the development of brain atrophy. Rowe et al. (1952) exposed rats, rabbits, guinea pigs, and monkeys to PCE vapors at levels of 100 to 400 ppm, 7 hour/day, 5 days/week for 6 months. Only guinea pigs showed adverse effects due to exposure. These effects included increased liver weights with some fatty degeneration, a slight increase in hepatic lipid content, and the presence of several small hepatic fat vacuoles. PCE also causes renal effects in rodents. Groups of rats and mice of each sex were exposed to PCE in corn oil by gavage 5 days/week for 78 weeks (NCI, 1977). Toxic nephropathy occurred at all dose levels in both sexes of rats and mice. PCE has been found to be fetotoxic, but not teratogenic at concentrations that are also maternally toxic (Schwetz, 1975). Fetotoxicity was usually expressed by decreased fetal weight and delayed skeletal ossification. There is some evidence that PCE causes adverse effects on reproductive systems. The finding of abnormal sperm in mice exposed to 500 ppm PCE is an indication of chemical effects on the sperm. However, definitive evidence that PCE or its metabolites reached germinal tissue and damaged DNA is not provided (U.S. EPA, 1985).

GENOTOXICITY

In vitro studies of PCE genotoxicity have been performed in prokaryotic, eukaryotic and mammalian cells. The results using prokaryotic systems were all negative, whereas in studies using yeast or mammalian cells, the results were mixed (Bronzetti et al., 1983; Price et al., 1978). NTP (1985) conducted inhalation carcinogenicity studies in F344/N rats and B6C3F1 mice of each sex for 6 hours/day, 5 days/week for 103 weeks. There were increases in mononuclear cell leukemia in rats and hepatocellular adenomas and carcinomas in mice. In chronic oral studies (NCI, 1977), PCE produced hepatocellular carcinomas in mice, but not in rats.

Epidemiological studies of dry-cleaning and laundry workers have determined significant excesses in mortality due to cancers of the lung, cervix, kidney, skin and colon (Blair et al., 1979; Kaplan, 1980). Although these studies suggest an association between chronic occupational exposure to PCE and increased cancer risk, the evidence is inconclusive, because workers were exposed to other solvents as well. Considering the inconclusive evidence for

carcinogenicity in humans, the U.S. EPA places PCE in Group B2, meaning that is considered a probable human carcinogen.

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THALLIUM

GENERAL BACKGROUND INFORMATION

Pure thallium is a soft bluish-white metal that is widely distributed in trace amount in the earth's crust. It is used in the manufacture of electronic devices, switches, and closures. It is also used to a limited extent in the manufacture of special glasses and for medical procedures that evaluate heart disease. Up until 1972, thallium was also used as a rat poison (ATSDR, 1991).

PHARMACOKINETICS

Thallium appears to be nearly completely absorbed from the gastrointestinal tract. No information was located on absorption following inhalation or dermal exposure. However, animal studies following intratracheal administration suggested that uptake through respiratory epithelium was rapid and complete. There is little information on the distribution of thallium in humans. Analysis of human tissues indicates that thallium is distributed throughout the body. The highest levels were found in the scalp hair, kidney, heart, bone, and spleen. In animals, the highest levels are found in the kidneys and liver. Excretion of thallium occurs by both the urinary and fecal routes (ATSDR, 1991).

HUMAN TOXICOLOGICAL PROFILE

Thallium is acutely lethal to humans following oral exposure at doses of 54-110 mg thallium/kg of body weight as thallium sulfate (Davis et al., 1981). The estimated lethal dose is approximately 14-15 mg/kg (Gosselin et al., 1984). Thallium compounds can affect the respiratory, cardiovascular, and gastrointestinal systems, the liver, kidneys and the male reproductive system. Alopecia (hair loss) and changes in the nervous system are characteristic of thallium exposure. A retrospective study was conducted which compared the incidence of congenital abnormalities in children born to mothers who had been exposed to thallium during pregnancy (Dolgener et al., 1983). The number of anomalies in the exposed group did not exceed the number of expected birth defects in the general population.

MAMMALIAN TOXICOLOGICAL PROFILE

In animals, the lowest doses showing lethality for a brief exposure period ranged from 5 to 30 mg/kg body weight for several species (Downs et al., 1960). Exposure to low doses (1.4 mg thallium as thallium sulfate/kg body weight/day) for longer durations (40-240 days) also cause death (Manzo et al., 1983). Electromyographic abnormalities without changes in

the myocardium are seen following a single oral dose (56 mg thallium/kg as thallium sulfate) in rabbits (Grunfeld et al., 1963). Parenteral injection in animals has been observed to cause liver effects. Thallium did not cause renal effects in rats following oral exposure, but parenteral exposure studies demonstrated that thallium affects the kidneys following subcutaneous administration. Rats exposed prenatally to 0.08 mg thallium/kg/day or greater during gestation evidenced impairment of learning. These effects occurred at dose levels below those at which other neurological effects (e.g structural and functional alterations of peripheral nerves) have been observed. Cultured rat embryos exposed to thallium at concentrations of 10, 30, or 100 ug/ml showed dose-related growth retardation at all levels showing embryotoxic effects (Anschutz et al., 1981). Administration by intraperitoneal injection to pregnant rats at a dose of 2.0 mg thallium/kg/day (as thallium sulfate) during gestation days 8-10 resulted in reduced fetal body weights, hydronephrosis, and the absence of vertebral bodies (Gibson and Becker, 1970).

GENOTOXICITY

Animal and bacterial assays suggest that thallium is genotoxic. Thallium-induced dominant lethal mutations in male rats in vivo. The overall embryonic mortality increased at doses of 0.04 ug thallium/kg day or greater as thallium carbonate. In vitro DNA damage tests employing rat embryo cells were positive (Zasukhina et al., 1983). Thallium enhanced viral-induced transformations in Syrian hamster embryo cells (Casto et al., 1979) and was positive in bacterial assays (Kanematsu et al., 1980). No studies are available on the carcinogenic effects of inhalation, oral or dermal exposure to thallium.

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TOLUENE

GENERAL BACKGROUND INFORMATION

Toluene is a clear, colorless organic liquid with a sweet smell and a high degree of lipid solubility. It is used as an industrial solvent/degreaser, as an intermediate in the manufacture of chemicals and pharmaceuticals, and is present as a component of gasoline and other fuels, paints, lacquers, adhesives, rubber and printing ink. Toluene is a volatile molecule with relatively low water solubility. It is flammable and may pose a fire hazard if handled improperly (ATSDR, 1989).

PHARMACOKINETICS

Toluene is readily absorbed by all routes of exposure (see section on Relative Absorption Factors). Once absorbed, it is rapidly distributed to all organ systems, including fetal tissue, with highest concentrations occurring in organs with high lipid content such as adipose tissue, brain and bone marrow. Toluene undergoes primarily oxidative metabolism to benzyl alcohol mediated by the mixed function oxidase enzyme system. Benzyl alcohol is further oxidized by alcohol and aldehyde dehydrogenase to produce benzoic acid which is primarily conjugated with glycine or glucuronic acid and excreted in urine as hippuric acids or benzoyl glucuronide. Toluene may also be excreted unchanged in exhaled air. Metabolism and excretion occurs rapidly, with the major portion occurring within 12 hours of exposure (Fishbein, 1985).

HUMAN TOXICOLOGICAL PROFILE

In humans, the most profound effects of toluene are on the central nervous system. Acute exposure results in reversible depression of the central nervous system, neurological dysfunction, impaired performance and narcosis. Chronic exposure has been reported to result in permanent central nervous system effects such as ataxia, tremors and impaired speech, hearing and vision (ATSDR, 1989). Toluene vapors cause irritation of the upper respiratory tract, mucous membranes and eyes, and may produce cardiac arrhythmias upon chronic exposure (Anderson et al., 1982). Reports of effects on the hematological system, liver, kidney, immune system, reproductive organs and the developing fetus are confounded by exposure to multiple solvents (ATSDR, 1989).

MAMMALIAN TOXICOLOGICAL PROFILE

Toluene has been demonstrated to produce similar effects in humans and animals. The major target organ following acute or chronic exposure is the central nervous system. Signs

of central nervous system damage include impaired motor abilities, narcosis, tremors, alterations in EEG activity, changes in the levels of brain neurotransmitters and morphological effects (ATSDR, 1989). High level inhalation exposure resulted in respiratory irritation and inflammation and pulmonary lesions (NTP, 1989). Toluene does not appear to be directly toxic to the cardiovascular system (Bruckner and Peterson, 1981). Decreased leukocyte counts were observed in dogs following exposure to toluene (Hobara et al., 1984). In addition, exposed mice exhibited increased susceptibility to respiratory infection (Aranyi et al., 1985). Hepatic effects appear to be relatively mild with reported increases in liver weight and minor ultrastructural changes (Ungvary et al., 1982). Renal toxicity has not been observed (NTP, 1989; Bruckner and Peterson, 1981). Studies with animals provide evidence that toluene may be a developmental toxicant. Exposure in utero resulted in skeletal anomalies, retarded skeletal growth and low fetal weights (Ungvary, 1985). No reproductive effects have been reported (API, 1985; NTP, 1989).

GENOTOXICITY

Available in vitro studies suggest that toluene is nongenotoxic (ATSDR, 1989). In vivo studies in animals provide additional supportive evidence (API, 1981). A small number of human studies have reported an increased incidence in chromosomal abnormalities, however, these studies are confounded by possible co-exposure to other chemicals (Schmid et al., 1985; Bauchinger et al., 1982). Other human studies have found no correlation between exposure to toluene and increased frequencies of chromosomal abnormalities (Haglund et al., 1980; Maki-Paakkanen et al., 1980).

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1,1,1-TRICHLOROETHANE

GENERAL BACKGROUND INFORMATION

1,1,1-Trichloroethane (also known as 1,1,1-TCA) is a colorless man-made chemical. It can be found in a liquid state, vapor, or dissolved in water or other chemicals. When found as a liquid, it evaporates rapidly and becomes a vapor in the air. 1,1,1-TCA has a sweet, sharp odor (ATSDR, 1990). 1,1,1-Trichloroethane is often used as a solvent to dissolve other substances such as glue or paint. Industrially, it is used to remove oil or grease from manufactured metal parts. Residentially, it is used for spot removal cleaners, aerosol sprays and glues. 1,1,1-Trichloroethane can be found in hazardous waste sites in the soil, water and in the air (ATSDR, 1990). It can be found in rivers, lakes, soil, drinking water, and drinking water from underground wells.

PHARMACOKINETICS

1,1,1-Trichloroethane is rapidly and completely absorbed by ingestion and inhalation (U.S. EPA, 1984). It distributes throughout the body and crosses the blood-brain barrier (U.S. EPA, 1984). If spilled topically, absorption via the skin would occur in small amounts because of quick evaporation into the air (U.S. EPA, 1984; ATSDR, 1990). Regardless of how 1,1,1-trichloroethane enters the body, most will quickly leave as exhalation occurs (ATSDR, 1990). What does not exit from expiration (metabolites) will be excreted through the urine and breath in a few days.

HUMAN TOXICOLOGICAL PROFILE

The toxic effects of 1,1,1-TCA are generally seen at concentrations well above those likely in an ambient environment. The most notable toxic effects of 1,1,1-TCA in humans are central nervous system depression, including anesthesia at very high concentrations, and impairment of coordination, equilibrium, and judgement at lower concentrations. Exposure to high concentrations may also result in cardiovascular effects, including premature ventricular contractions, decreased blood pressure and sensitization of the heart to epinephrine-induced arrhythmias, leading possibly to cardiac arrest (U.S. EPA, 1985; ATSDR, 1990). Acute exposure to minimal concentrations of 1,1,1-trichloroethane did not produce respiratory or lung volume effects (Dornette, 1960; Torkelson et al., 1958).

MAMMALIAN TOXICOLOGICAL PROFILE

Similar effects as noted above are observed in animals exposed to 1,1,1-TCA. In addition, animal experiments investigating the influence of 1,1,1-TCA on liver and kidney function yield conflicting results highly dependent on species, doses, and treatment schedules. Fatty changes in rodent livers following exposure by inhalation have been reported (U.S. EPA, 1985).

GENOTOXICITY

No studies were located regarding genotoxic effects in humans or animals following exposure to 1,1,1-trichloroethane (ATSDR, 1990). Evidence for or against an association between exposure to 1,1,1-TCA and cancer in humans has not been reported. Animal studies fail to provide any definitive link between exposure and carcinogenicity (ATSDR, 1990).

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TRICHLOROETHYLENE

GENERAL BACKGROUND INFORMATION

Trichloroethylene (TCE) is widely used as an industrial solvent, particularly in metal degreasing, which consumes about 90% of TCE produced annually in the U.S. TCE is also used for dry-cleaning, as a low-temperature heat exchange fluid, as a fumigant, as a diluent in paints and adhesives, in aerospace operations, and in textile processing. Previously, TCE was used as an extractant in food-processing. These uses were discontinued in 1975 due to evidence of possible carcinogenic activity. Its earlier use in anesthetics was also discontinued (IRP, 1985).

PHARMACOKINETICS

Absorption of TCE from the gastrointestinal and respiratory tracts is extensive. TCE is extensively metabolized in humans to trichloroethanol, trichloroethanol glucuronide, and trichloroacetic acid. Although the liver is the primary site of TCE metabolism, there is evidence for extrahepatic metabolism in the lungs and kidneys (ATSDR, 1988).

HUMAN TOXICOLOGICAL PROFILE

TCE is assumed to be responsible for the deaths of four men employed at degreasing operations using TCE as the solvent (Kleinfeld and Tabershaw, 1954). Toxicological analysis revealed TCE in varying concentrations in various tissues. Kleinfeld and Tabershaw (1954) reported that, despite treatment, a man died 11 days after he accidentally drank an unknown quantity of TCE. TCE has been shown to affect the central nervous system. Short-term exposure to high concentrations of TCE caused dizziness, headache, nausea, confusion, facial numbness, blurred vision, and, at very high levels, unconsciousness. Longer exposures cause ataxia, decreased appetite, sleep disturbances, and trigeminal neuropathy (U.S. EPA, 1985). Information regarding hepatotoxicity in humans is limited and derived from acute overexposures. U.S. EPA (1985) has concluded that it is unlikely that chronic exposure to trichloroethylene at concentrations found or expected in ambient air would result in liver damage.

MAMMALIAN TOXICOLOGICAL PROFILE

In laboratory animals, the acute toxicity of trichloroethylene is low. Oral LD₅₀ values of 4920 mg/kg in the rat, 3200 mg/kg in the mouse and 2800 mg/kg in the dog have been reported. In a study by Baker (1958), several dogs died within 20 minutes of being exposed to TCE at 30,000 ppm. Rats exposed to 20,000 ppm for 5 hours died (Adams, 1951). A 2-year study

in rats conducted by the NTP (1986a) showed decreased survival due to TCE treatment. Deaths were attributed to toxic nephrosis. Behavioral changes were observed in rats at TCE vapor concentrations as low as 100 ppm (Silverman and Williams, 1975). Liver enlargement is the most commonly observed hepatic effect seen in TCE-exposed animals (Kjellstrand et al., 1983). Mice, especially males, appear to be particularly sensitive to the hepatotoxic effects of TCE. The only reproductive effects observed were reduced testis and epididymis weights in rats exposed to dietary TCE (NTP, 1986b). There were no effects of reproductive system histology, fertility, or other reproductive performance parameters in treated males or females in these studies.

GENOTOXICITY

Perocco and Prodi (1981) found positive results for unscheduled DNA synthesis both with and without metabolic activation in human lymphocytes in vivo. Another study reported a significant increase in sister chromatid exchange in six workers exposed to TCE (Gu et al., 1981). In vitro mutagenicity tests in bacteria, yeasts, and molds demonstrated weak positive responses. Most of these tests required metabolic activation of the compound (Crebelli et al., 1985). TCE has been shown to be carcinogenic in animals. Inhalation and oral exposure produced liver and lung tumors in mice and kidney adenocarcinomas, testicular Leydig cell tumors, and possibly leukemia in rats. These studies are deemed sufficient to place TCE in CAG classification B2, probable human carcinogen (U.S. EPA, 1987). Further support that TCE is a probable human carcinogen comes from studies that indicate that metabolism is qualitatively similar in humans and test animals (U.S. EPA, 1987). The available carcinogenicity studies indicate that mice are more susceptible to TCE carcinogenicity than the rat. Factors contributing to this difference may be an increased rate of metabolic conversion to trichloroacetic acid in mice, and the more pronounced trichloroacetic acid-mediated peroxisomal proliferation and cell proliferation in mice (Elcombe et al., 1985). The peroxisomal proliferation may lead to an increase in the reactive oxygen species and DNA damage, which may lead to hepatocellular carcinoma.

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VINYL CHLORIDE

GENERAL BACKGROUND INFORMATION

About 90% of the vinyl chloride produced in the U.S. is used to manufacture polyvinyl chloride (PVC) and other vinyl polymers. The remainder is used to synthesize 1,1,1-trichloroethane. The major uses of PVC are in the building and construction industries, in consumer goods, packaging and electrical wire insulation. PVC is also used in packaging, such as plasticized film, bottles and bottle-cap liners and gaskets (IRP, 1985).

PHARMACOKINETICS

Respiratory and gastrointestinal absorption of vinyl chloride is rapid and nearly complete. Distribution may be widespread with the highest concentration of the parent compound located in the fat. Metabolism and excretion occur rapidly. The highest levels of excretory products are located in the liver and kidney (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Several epidemiologic studies have associated occupational exposure with impaired liver function and biochemical or histological evidence of liver damage (U.S. EPA, 1985a,b). Symptoms and signs of liver disease associated with occupational exposure to vinyl chloride include pain or discomfort, hepatomegaly, portal hypertension, thrombocytopenia, esophageal varices (Lee et al., 1977). Acute toxicity at high levels has resulted in lethality among occupationally exposed workers. Death appeared to be due to narcosis (U.S. EPA, 1985a). Acute inhalation exposure to high levels of vinyl chloride leads to CNS effects. Exposures to 8,000 to 20,000 ppm have been associated with dizziness, giddiness, euphoria, ataxia, headache, and narcosis (Nicholson et al., 1975; Lester et al., 1963). Dinceva et al. (1985) reported electroencephalogram changes that they thought were indicative of early evidence of neurotoxicity in workers exposed to vinyl chloride along with other organic solvents. Vinyl chloride disease is the name given to the total clinical syndrome associated with occupational exposure. It includes a syndrome known as acroosteolysis or dissolution of the ends of the distal phalanges of the hands, circulatory disturbance in the extremities, Raynaud syndrome, scleroderma, hematologic effects, and lung and liver effects (ATSDR, 1989).

MAMMALIAN TOXICOLOGICAL PROFILE

Patty et al. (1930) reported that narcosis and death occurred within 30 to 60 min in guinea pigs exposed to 10% vinyl chloride. U.S. EPA (1985a) reviewed a number of acute studies in animals and reported 2 hour LC_{50} values ranging from 117 to 500 ppm for mice to 230 to 800 ppm for rabbits. Liver injury is observed in chronically-exposed animals. A study by the Dow Chemical Company (1984) in rats chronically-exposed to vinyl chloride through inhalation established 0.13 mg/kg/day as NOAEL, and 1.3 mg/kg/day as a LOAEL for hepatotoxicity. Animals exposed orally or by inhalation manifest noncancerous liver effects similar to those seen in humans; but other effects seen in humans, such as acroosteolysis, Raynaud syndrome, and scleroderma, have not been reproduced in animals (ATSDR, 1989).

GENOTOXICITY

Vinyl chloride is mutagenic in *S. typhimurium* in numerous studies (ATSDR, 1989). Vinyl chloride was positive for recessive lethal effects but negative for dominant lethal effects, chromosomal translocation, and sex chromosome loss in *D. melanogaster* (Verburgt and Vogel, 1977). Positive results were obtained in mutation and cell transformation tests and in chromosomal aberration tests in vivo and in vitro mammalian systems (Styles, 1977; Laib et al., 1985; Anderson and Richardson, 1981). Genotoxicity studies of vinyl chloride in humans include a large number of chromosomal aberration tests in the peripheral lymphocytes of occupationally exposed workers. These tests have all been positive (ATSDR, 1989). Anderson et al. (1980) observed an increase in lymphocytes with chromosomal aberrations at exposure levels estimated at 50 ppm.

Maltoni and associates (1981) conducted vinyl chloride carcinogenicity studies in animals. They exposed rats, mice and hamsters for 4 hours/day, 5 days/week for one year to vapor concentrations of 1 ppm to 30,000 ppm or to 0.03 to 50 mg/kg bw vinyl chloride in olive oil by ingestion, 5 days/week for one year. Liver angiosarcomas were observed in all the animals tested. Bi et al. (1985) exposed adult male Wistar rats to 0, 10, 100, or 3000 ppm, 6 hours/day, 6 days/week for up to 12 months to evaluate effects on the testes. Relative testicular weight was significantly reduced at 100 or 3000 ppm. Vinyl chloride workers are at increased risk for developing cancer. Liver angiosarcomas, brain, skin and lung tumors, and tumors of the lymphatic and blood-forming systems are some of the cancers seen in exposed workers (Tamburro, 1984). Individuals residing near PVC processing plants may also be at risk. Five cases of angiosarcoma of the liver were diagnosed in persons living in the vicinity of vinyl chloride fabrication and polymerization plants for 8 to 62 years prior to the diagnosis of the disease (U.S. EPA, 1980).

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XYLENES

GENERAL BACKGROUND INFORMATION

Xylenes are colorless liquid organic molecules with a sweet odor and a high degree of lipid solubility. There are three isomers of xylene: meta- ortho- and para-xylene (m-, o- and p-xylene, respectively). The term "total xylenes" is used to designate a mixture of the three possible isomers, in any proportions. They are commonly used as industrial solvents, as components of paints, varnishes, cleaners, degreasers and gasoline and as chemical intermediates in the manufacture of other chemicals, plastics and synthetic fibers. Xylenes are volatile molecules and therefore, evaporate quickly. They are also flammable and may pose a fire hazard if handled improperly (ATSDR, 1990).

PHARMACOKINETICS

Xylenes are readily absorbed by all routes of exposure (see section on Relative Absorption Factors). Xylenes are very soluble in blood and therefore are absorbed easily into the systemic circulation during exposure (Astrand, 1982). Following absorption, distribution occurs rapidly to all organs, including fetal tissue, with greatest distribution occurring to organs having a high lipid content, such as adipose tissue, bone marrow and brain (Astrand, 1982; Engstrom and Bjurstrom, 1978; Riihimaki et al., 1979). In humans, xylenes are primarily metabolized by the mixed function oxidase enzyme system to methylbenzyl alcohols which are further oxidized by alcohol and aldehyde dehydrogenase to yield methyl benzoic acids. The acids are readily conjugated and excreted in urine (Fishbein, 1985). In addition, a small percentage (3-6%) is exhaled unchanged due to the volatile nature of these compounds.

HUMAN TOXICOLOGICAL PROFILE

Human data suggests that the three xylene isomers all produce qualitatively similar effects, although the individual isomers are not necessarily equal in potency with regard to a given effect (ATSDR, 1990). Exposure, by any route, results in primarily central nervous system effects that may include headaches, nausea, mental confusion, narcosis, impaired learning and memory, dizziness, tremors, unconscienceness and coma, depending on dose and length of exposure. High doses may result in death. The respiratory system may also be a target of xylene toxicity in humans, producing respiratory tract irritation, pulmonary edema and inflammation after inhalation. Ocular irritation may result following exposure to xylene vapors. Skin irritation, dryness and scaling may result following dermal exposure. Limited data are available concerning effects of exposure on the hepatic, renal, cardiovascular,

musculoskeletal or hematological system. Insufficient information is available regarding the developmental and reproductive toxicity of xylenes in humans.

MAMMALIAN TOXICOLOGICAL PROFILE

Exposure to xylenes produces similar effects in humans and laboratory animals. The central nervous system is the primary target for both short-term and long-term exposures. Respiratory effects are observed following inhalation exposure. Data from animal studies provide limited evidence that xylene may produce cardiovascular effects (arrhythmias, atrial fibrillation and alterations in blood vessels and blood flow) (Morvai et al., 1976, 1987), hepatic effects (enzyme induction, increased liver weight, ultrastructural alterations) (Condie et al., 1988; Elovaara et al., 1980; Elovaara, 1982) and renal effects (enzyme induction, renal atrophy, tubular alterations) (Condie et al., 1988; Elovaara, 1982; Toftgard and Nilsen, 1982). These results suggest that humans might be at increased risk of developing such effects following exposure. Findings in animal studies suggest that xylenes may produce developmental defects including increased fetal death, decreased fetal weight, delayed skeletal development and gross anomalies (Marks et al., 1982; Ungvary et al., 1980). No animal data exists suggesting effects on reproductive organs, the musculoskeletal system or hematological system.

GENOTOXICITY

Xylenes have been tested for genotoxicity in a variety of in vitro and in vivo assays. Results of the various assays indicate that xylenes are nongenotoxic following in vitro and in vivo exposure (ATSDR, 1990). No evidence of carcinogenicity exists in humans or laboratory animals (ATSDR, 1990).

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ZINC

GENERAL BACKGROUND INFORMATION

Zinc is used most commonly as a protective coating for other metals and in alloys such as bronze and brass. Zinc is emitted to the atmosphere during mining and refining, manufacturing processes, and combustion of zinc-containing materials. Zinc is an essential trace element in nutrition and is found in many foods (ATSDR, 1989).

PHARMACOKINETICS

It has been reported that about 20 to 30 percent of ingested zinc is absorbed and the mechanism may be homeostatically controlled and carrier-mediated. When zinc levels in the body are sufficient to sustain normal physiological functions, zinc absorption decreases. Absorption occurs by the inhalation and dermal routes as well. Once absorbed, zinc is distributed throughout the body where it is used as an essential cofactor in many enzyme systems. Excretion occurs primarily through the feces (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Zinc compounds are of relatively low toxicity by ingestion. In humans, exposure to 2 g or more of zinc produces symptoms of fever, nausea, vomiting, stomach cramps, and diarrhea 3-12 hours after ingestion. Zinc chloride is a primary component of smoke bombs, and pathologic changes in humans due to acute inhalation exposure to ZnCl include laryngeal, tracheal, and bronchial mucosal edema and ulceration, interstitial edema, interstitial fibrosis, alveolar obliteration and bronchiolitis obliterans. Severe acute injury is associated with a high mortality (Matarese and Matthews, 1986). Metal fume fever results from occupational inhalation of freshly formed fumes of zinc oxides. It is characterized by transient chills and fever, profuse sweating, and weakness some hours after exposure. The fumes usually consist of extremely fine particles containing other metals in addition to zinc. The very small size (submicronic) of the fume particles with their potential for alveolar deposition is thought to be an important aspect of this phenomenon. It has generally been estimated that fume fever does not occur at zinc oxide levels less than 15 mg/m^3 although some occurrence of fume fever has been reported at levels as low as 5 mg/m^3 . This occupational hazard is not considered to be a general public health problem (U.S. EPA, 1987a; U.S. EPA, 1987b). Poorly ionized zinc compounds have low dermal toxicity and have been used therapeutically and cosmetically for many years as mild astringents, antiseptics and perspirants (Gilman et al., 1985).

MAMMALIAN TOXICOLOGICAL PROFILE

The highly ionizable zinc salts such as zinc chloride can be acutely toxic. Acute toxicity in laboratory animals was reported to be 250 mg/kg (LD_{50}) for the guinea pig. A TC_{50} of 4800 mg/m³ for 30 minutes was calculated for humans (Clayton and Clayton, 1981).

Zinc has a low oral chronic toxicity. In a study involving dogs and cats, 175 to 1000 mg/kg per day of ZnO, administered orally for 3 to 53 weeks, was tolerated. Some of the dogs showed glucosuria and some of the cats showed fibrous degeneration of the pancreas. A number of other animal feeding studies demonstrate the low oral toxicity of zinc (Clayton and Clayton, 1981; U.S. EPA, 1987a).

Generally adverse but minor effects have been demonstrated in guinea pigs inhaling large amounts (1-5 mg/m³) of zinc oxides (Lam et al., 1982,1985; Amdur et al., 1982). Lam et al. (1985) measured pulmonary function in guinea pigs exposed to zinc oxide fume at 5 mg/m³ three hours daily for a period of six days. Vital capacity, functional residual capacity, alveolar volume, and single breath diffusive capacity for carbon monoxide decreased following the final exposure and did not return to normal after 72 hours. Flow resistance increases, and decreases in compliance and total lung capacity returned to normal after this period. Fibroblasts in interstitial infiltrates (including a fibrotic reaction) were observed. It was concluded that pulmonary changes may occur with relatively few exposures at the workplace threshold limit value.

Zinc does not appear to be teratogenic except perhaps at very high doses; intraperitoneal injections of relatively large doses (20 mg/kg) in mice during pregnancy results in some malformations in fetal ossifications (Chang et al., 1977).

GENOTOXICITY

Various studies have indicated that zinc is not mutagenic. In vitro analyses of zinc chloride demonstrated that the fidelity of DNA synthesis was unaffected (Sirover and Loeb, 1976a,b; Miyaki et al., 1977). Zinc industry employees have shown a greater number of chromosomal aberrations in peripheral blood lymphocytes than did controls (Bauchinger et al., 1976). However, these workers were also exposed to other agents known to cause chromosome structural alterations (Leonard, 1985). There is no evidence that the inhalation, ingestion or parenteral administration of zinc induces the formation of tumors.

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APPENDIX C

RELATIVE ABSORPTION FACTORS

(RAFs)

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RELATIVE ABSORPTION FACTORS

(RAFs)

The derivation of a Relative Absorption Factor (RAF) for a chemical by a specific route and medium of exposure involves two basic steps:

- (1) the identification of derived route- and medium-specific absorption efficiencies from the literature for the chemical and
- (2) the comparison of the absorption efficiency by the route and medium of exposure with the absorption efficiency by the route and medium in the study used as the basis for the derivation of the toxicity value.

The identification of the route- and medium-specific absorption efficiencies was accomplished through a literature search and data collection exercise.

For the oral route of exposure, the highest reported absorption efficiency for the medium of interest was taken as the most appropriate value.

For the dermal route of exposure, a 24-hour, non-occluded exposure was selected as the most appropriate scenario. All the dermal absorption efficiencies were adjusted to comply with this selection.

For the inhalation route of exposure, the steady state or equilibrium absorption efficiency was selected as the most appropriate value as the exposure scenarios of interest in the *Residential ShortForm* are not acute in nature.

When no data existed for the specific medium of interest, a value was selected from the literature which was derived by the same route (but different medium). When no data existed for the specific route in question, the absorption efficiency for a different substance with similar chemical and physical properties was used.

Once the appropriate route- and medium-specific absorption efficiencies were obtained, the toxicity values were examined and the RAFs were derived.

When the toxicity value represents an APPLIED dose (or concentration), the RAF is calculated as the ratio of the absorption efficiency by the route and medium of the exposure scenario of interest and the absorption efficiency by the route and medium of the study used as the basis for the derivation of the toxicity value.

When the toxicity value represents an ABSORBED dose (or concentration), the RAF is simply the absorption efficiency of the chemical by the route and medium of concern.

The risk assessor is referred to the following documents for a more detailed discussion of the *Relative Absorption Factor*.

Guidance for Disposal Site Risk Characterization and Related Phase II Activities - In Support of the Massachusetts Contingency Plan, Massachusetts Department of Environmental Quality Engineering [Policy No. WSC/ORS-141-89] (1989) APPENDIX B.

Risk Assessment Guidance For Superfund: Volume I -- Human Health Evaluation Manual (Part A), U.S. Environmental Protection Agency, Office of Emergency and Remedial Response [EPA 540/1-89/002] (December 1989) APPENDIX A.

**The following pages describe the derivation of the
Relative Absorption Factors for each of the
chemicals contained in the *Residential ShortForm***

*These values will be updated periodically, and the risk
assessor should use the most current values.*

The following table of references is reproduced from Table VII-1, and is included here to support the chemical specific toxicity information which appear at the beginning of each of the following sections and which are used to develop the RAFs.

References for the *ShortForm* Toxicity Values

<u>Reference #</u>	<u>Description</u>
1.	U.S. EPA <i>Integrated Risk Information System</i> (IRIS). On-line search: current as of September 2, 1992.
1.a.	The oral Carcinogenic Potency Value from IRIS is used as a dermal CPV.
1.c.	The chronic inhalation RfC (from IRIS) has been used here as a subchronic inhalation RfC equivalent.
1.d.	This toxicity value for CHROMIUM is taken from the IRIS file for hexavalent chromium (Cr VI).
1.e.	The chronic oral RfD (from IRIS) has been used here as a subchronic oral RfD equivalent.
1.f.	This oral Carcinogenic Potency Value equivalent for arsenic is back-calculated from a drinking water Unit Risk value from IRIS.
1.g.	This Carcinogenicity Potency Value or Unit Risk for benzo[a]pyrene (from IRIS) has been applied to the seven PAH compounds which are designated as category A, B1, B2 or C carcinogens.
2.	U.S. EPA <i>Health Effects Assessment Summary Tables</i> (HEAST), Annual FY-1992. [OERR 9200.6-303 (92-1), NTIS No. PB92-921199] March, 1992.
2.a.	The oral Carcinogenic Potency Value from HEAST is used as a dermal CPV.
2.b.	This subchronic oral RfD (from HEAST) for naphthalene has been used as the subchronic oral RfD equivalent for all PAH compounds for which subchronic oral RfDs are unavailable.
2.c.	The chronic inhalation RfC (from HEAST) has been used here as a subchronic inhalation RfC equivalent.
2.d.	The chronic oral RfD for food (from HEAST) has been used as the oral RfD for cadmium.
2.e.	The chronic oral RfD for cadmium (from HEAST) has been used here as a subchronic oral RfD equivalent.
2.f.	The chronic oral RfD for naphthalene (from HEAST) has been used as the chronic RfD equivalent for all PAH compounds for which chronic oral RfDs are unavailable.
2.g.	This toxicity value for CHROMIUM (taken from HEAST) is for hexavalent chromium (Cr VI).
2.h.	This Carcinogenic Potency Value or Unit Risk was taken from a fact sheet distributed by the U.S. EPA Superfund Health Risk Technical Support Center at ECAO-Cincinnati.
2.i.	The oral Carcinogenic Potency Value (from the ECAO-Cincinnati fact sheet) is used as a dermal CPV.

3. Allowable Threshold Concentrations (ATCs) from MA DEQE (1989a), *Guidance for Disposal Site Risk Characterization and Related Phase II Activities - In Support of the Massachusetts Contingency Plan*, Appendix J.
- 3.a. The chronic inhalation ATC (from MA DEQE, 1989a) has been used here as a subchronic inhalation ATC equivalent.
- 3.b. The ATC for "total concentration of naphthalene and 2-methylnaphthalene" is used here as the ATC for this chemical.
- 3.c. The chronic inhalation ATC for naphthalene has been used as the chronic inhalation RfC equivalent for all PAH compounds for which chronic inhalation RfCs are unavailable.
- 3.d. The chronic inhalation ATC for naphthalene has been used as the subchronic inhalation RfC equivalent for all PAH compounds for which subchronic RfCs are unavailable.
4. Developed for the *Residential ShortForm* by MA DEP staff. Documentation of this value may be found in APPENDIX D.
- NC Not Considered to be Carcinogenic by this Exposure Medium

ACENAPHTHENE

CAS #: 83329

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose: 0.6 mg/kg/day (2)****Chronic Oral Reference Dose: 0.06 mg/kg/day (1)****Subchronic Inhalation Reference Concentration: Not Volatile****Chronic Inhalation Reference Concentration: Not Volatile****Oral Cancer Potency Factor: NC****Inhalation Cancer Unit Risk: Not Volatile**

No specific quantitative information found on oral or dermal inhalation route. Assume same as B[a]P.

The oral and dermal chronic reference dose for acenaphthene is based on an oral gavage study in mice. In this study, an applied dose was used.

ACENAPHTHENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

The oral and dermal subchronic reference dose for acenaphthene is based on an oral gavage study in mice. In this study, an applied dose was used.

ACENAPHTHENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

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ACENAPHTHYLENE

CAS #: 208968

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose: 0.04 mg/kg/day (2b)****Chronic Oral Reference Dose: 0.04 mg/kg/day (2f)****Subchronic Inhalation Reference Concentration: Not Volatile****Chronic Inhalation Reference Concentration: Not Volatile****Oral Cancer Potency Factor: NC****Inhalation Cancer Unit Risk: Not Volatile**

No specific quantitative information found on oral or dermal route. Assume same as B[a]P.

The oral and dermal chronic reference dose for acenaphthylene is based on an oral naphthalene gavage study in rats. In this study, an applied dose was used.

ACENAPHTHYLENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

The oral and dermal subchronic reference dose for acenaphthylene is based on a naphthalene oral gavage study in rats. In this study, an applied dose was used.

ACENAPHTHYLENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

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ANTHRACENE

CAS #: 120127

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 3 mg/kg/day (2)

Chronic Oral Reference Dose: 0.3 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: Not Volatile

No specific quantitative information found on oral or inhalation route. Assume same as B[a]P.

Percutaneous absorption of ¹⁴C-anthracene was estimated to be 52% of the applied dose (Yang et al., 1986). Assume this is reduced by 50% (to 26%) when compound is applied as a complex environmental mixture.

Yang, J.J., Roy, T.A. and Mackerer, C.R. (1986) *Percutaneous Absorption of Anthracene in the Rat: Comparison of in Vivo and in Vitro Results*. Toxicol. Ind. Health. 2:79-84.

The oral and dermal chronic reference dose for anthracene is based on an oral gavage study conducted in mice. In this study, an applied dose was used.

ANTHRACENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.26}{0.91} = 0.29$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

The oral and dermal subchronic reference dose for anthracene is based on an oral gavage study conducted in mice. In this study, an applied dose was used.

ANTHRACENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.26}{0.91} = 0.29$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.0003 mg/kg/day (2)

Chronic Oral Reference Dose: 0.0003 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: $1.8 \text{ (mg/kg/day)}^{-1}$ (1f)

Inhalation Cancer Unit Risk: Not Volatile

Human studies support the assumption that the soluble salts of inorganic arsenic are almost completely absorbed by the oral route. Literature sources cite an absorption efficiency of 98% for arsenic in humans and laboratory animals (Vahter, 1983; EPA, 1984, 1985; Goyer, 1986).

Vahter, M. (1983) *Metabolism of Arsenic*. In: Fowler, B.A., ed. Biological and Environmental Effect of Arsenic. New York: Elsevier, pp. 171-198.

U.S. Environmental Protection Agency (U.S. EPA) (1985) Health Advisories for 52 Chemicals Which Have Been Detected in Drinking Water. PB86-118338.

U.S. Environmental Protection Agency (U.S. EPA) (1984) Health Assessment Document for Inorganic Arsenic. Final report. Research Triangle Park, NC: Environmental Protection Agency. EPA 600/8-83-021F.

Goyer, R.A. (1986) Casarett and Doull's Toxicology. (C.D. Klaassen, M.O. Amdur and J. Doull, Eds.) 3rd ed., pp. 582-635, MacMillan, New York.

No quantitative studies were located to evaluate the dermal absorption of arsenic compounds. However, clinical symptoms of arsenic poisoning have been reported in humans after accidents where the only route of exposure was through the skin, suggesting that dermal absorption does occur. An absorption efficiency of 3% may be considered a conservative upper-bound based on EP toxicity studies where the extraction of arsenic from soil (Ph 5, 24 hours) averaged 3%.

The oral and dermal cancer potency value for arsenic is based on a drinking water ingestion study in humans. In this study, an applied dose was used.

ARSENIC RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.98}{0.98} = 1$	$\frac{0.03}{0.98} = 0.03$	$\frac{0.98}{0.98} = 1$	$\frac{0.98}{0.98} = 1$

The oral and dermal chronic reference dose for arsenic is based on a drinking water ingestion study in humans. In this study, an applied dose was used.

ARSENIC RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.98}{0.98} = 1$	$\frac{0.03}{0.98} = 0.03$	$\frac{0.98}{0.98} = 1$	$\frac{0.98}{0.98} = 1$

The oral and dermal subchronic reference dose for arsenic is based on a drinking water ingestion study in rats. In this study, an applied dose was used.

ARSENIC RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.98}{0.98} = 1$	$\frac{0.03}{0.98} = 0.03$	$\frac{0.98}{0.98} = 1$	$\frac{0.98}{0.98} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.05 mg/kg/day (4)

Chronic Oral Reference Dose: 0.005 mg/kg/day (4)

Subchronic Inhalation Reference Concentration: 32 $\mu\text{g}/\text{m}^3$ (4)

Chronic Inhalation Reference Concentration: 9 $\mu\text{g}/\text{m}^3$ (3)

Oral Cancer Potency Factor: 0.029 (mg/kg/day)⁻¹ (1)

Inhalation Cancer Unit Risk: 0.0000083 ($\mu\text{g}/\text{m}^3$)⁻¹ (1)

The oral absorption efficiency of pure benzene is estimated to be essentially 100% based on rabbit data in which 100% of an oral dose was either metabolized or exhaled unchanged (Sabourin et al., 1986). The oral bioavailability of benzene was slightly but not significantly increased by adsorption to clay soil (Turkall, et al., 1988). Human (Parke and Williams, 1953) and animal studies suggest that virtually all (100%) of an oral dose of benzene is absorbed.

Parke, D.V. and Williams, R.T. (1953) *Studies in Detoxication*. 49. *The Metabolism of Benzene Containing [¹⁴C] Benzene*. *Biochem. J.* 54:231-238.

Sabourin, P., Chen, B., Henderson, R. Lucier, G. and Birnbaum, L. (1986) *Effect of Dose on Absorption and Excretion of ¹⁴C-Benzene Administered Orally or by Inhalation*. *The Toxicologist*. 6:163.

Turkall, R.M., Skowronski, G., Gerges, S., Von Hagen, S. and Abdel-Rahmen, M.S. (1988) *Soil Adsorption Alters Kinetics and Bioavailability of Benzene in Orally Exposed Male Rats*. *Arch. Environ. Contam. Toxicol.* 17:159-164.

For dermal absorption, the controlling factor is contact time with the skin. One study (Susten et al., 1990) estimated the non-occluded dermal absorption of benzene in hairless mice to be approximately 1% of the applied dose in 4 hour (or 6% in 24 hours), with volatilization occurring rapidly. In a second study (Susten et al., 1985), the dermal absorption efficiency (non-occluded) of benzene was 1% of the applied dose in 2.5 hours (or 10% in 24 hours). In an occluded study (Lam and Bisgaard, 1989), the dermal absorption efficiency of 1,3-diaminobenzene was 100% of the applied dose in 24 hours for aqueous solutions and hydrogen peroxide-based solutions of this benzene analog. This suggests that the dermal absorption of benzene is highly dependent on whether an occluded or non-occluded study design is utilized. An average non-occluded dermal absorption efficiency (24 hour) of 10% was selected as a protective estimate from these studies while an occluded 24-hr dose would be absorbed 100%. The dermal bioavailability of benzene was slightly reduced by its adsorption to soil (Skowronski, et al., 1988). The

dermal absorption efficiency of soil-adsorbed benzene was estimated to be approximately 12% in 36 hours (8% in 24 hours) in a non-occluded study.

Agency for Toxic Substances and Disease Registry (ATSDR) (1989) Toxicological Profile for Benzene. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. pp. 36-38.

Skowronski, G.A., Turkall, R.M. and Abdel-Rahman, M.S. (1988) *Soil Adsorption Alters Bioavailability of Benzene in Dermal Exposed Male Rats*. *Am. Ind. Hyg. Assoc. J.* 49:506-511.

Susten, A.S., Niemeier, R.W. and Simon, S.D. (1990) *In Vivo Percutaneous Absorption Studies of Volatile Organic Solvents in Hairless Mice II. Toluene, Ethylbenzene and Aniline*. *J. Appl. Toxicol.* 10:217-225.

Lam, H.R. and Bisgaard, H.C. (1989) *Percutaneous Absorption, Biotransformation, Retention and Excretion of 1,3-Diaminobenzene in the Rat*. *Fd. Chem. Toxicol.* 27:741-749.

The oral and dermal cancer potency value for benzene was derived from a human inhalation study. In this study, an absorbed dose was used. The RAFs for all scenarios are therefore the absorption efficiencies of benzene by the route in question.

BENZENE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.08	1	1

The oral and dermal chronic reference dose for benzene was derived from an animal inhalation study. An absorption efficiency of 50% was used to calculate an absorbed dose. The RAFs for all pathways are the absorption efficiencies of benzene by the route in question.

BENZENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.08	1	1

The oral and dermal subchronic reference dose for benzene was derived from an animal inhalation study. An absorption efficiency of 50% was used to calculate an absorbed dose. The RAFs for all scenarios are the absorption efficiencies of benzene by the route in question.

BENZENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.08	1	1

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BENZO[a]ANTHRACENE

CAS #: 56553

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose:** 0.04 mg/kg/day (2b)**Chronic Oral Reference Dose:** 0.04 mg/kg/day (2f)**Subchronic Inhalation Reference Concentration:** Not Volatile**Chronic Inhalation Reference Concentration:** Not Volatile**Oral Cancer Potency Factor:** $7.3 \text{ (mg/kg/day)}^{-1}$ (1g)**Inhalation Cancer Unit Risk:** Not Volatile

No specific quantitative information found on oral or dermal route. Assume same as B[a]P.

The oral and dermal cancer potency value for benzo[a]anthracene is based on a dietary study in which B[a]P was administered to mice. In this study, an applied dose was used.

BENZO[a]ANTHRACENE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

The oral and dermal chronic reference dose for benzo[a]anthracene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

BENZO[a]ANTHRACENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

The oral and dermal subchronic reference dose for benzo[a]anthracene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

BENZO[a]ANTHRACENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.04 mg/kg/day (2b)

Chronic Oral Reference Dose: 0.04 mg/kg/day (2f)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: $7.3 \text{ (mg/kg/day)}^{-1}$ (1)

Inhalation Cancer Unit Risk: Not Volatile

The oral absorption of ^{14}C -labeled B[a]P, dissolved in peanut oil and administered by gavage, was studied in rats (Hecht et al., 1979). Absorption was determined by recovery of label in urine and feces. Unchanged B[a]P recovered in feces was estimated at 9% of the total dose, with all other fecal radioactivity (85% of applied dose) recovered as metabolites. This suggests an oral absorption efficiency of 91%.

Hecht, S.S., Grabowski, W. and Groth, K. (1979) *Analysis of Feces for B[a]P After Consumption of Charcoal-Broiled Beef by Rats and Humans*. *Food Cosmet. Toxicol.* 17:223-227.

The percutaneous absorption of ^{14}C -B[a]P was studied in vivo in Swiss Webster mice (Sanders et al., 1986) and in Sprague-Dawley rats (Yang et al., 1986). Absorption was determined by analyzing radioactivity in urine, feces and tissues, and by analysis of residual label at the site of application. Dermal absorption efficiency was measured as 40% (in mice) and 6% (in rats) in 24 hrs. The higher value of 40% is selected as a protective estimate for human dermal exposure to pure compound. In vitro estimates are lower, ranging from 0.1%-15% in humans and animals (Kao et al., 1985; Kao et al., 1988) and are not considered applicable to human exposure. The in vivo percutaneous absorption of soil-adsorbed B[a]P was determined in rats by Yang et al. (1989). The range of absorbed doses was 1.3% - 9.2% depending on the amount of soil applied. More efficient absorption occurred at lower soil application rates. Wester et al. (1990) confirms a low absorption for soil-associated B[a]P in the rhesus monkey with a range of 9% - 18%. The upper limit of 18% is selected as a protective estimate for human exposure to B[a]P contaminated soil.

Kao, J., Hall, J. and Helman, G. (1988) *In Vitro Percutaneous Absorption in Mouse Skin: Influence of Skin Appendages*. *Toxicol. Appl. Pharmacol.* 94: 93-103.

Kao, J.K., Patterson, F.K., and Hall, J. (1985) *Skin Penetration and Metabolism of Topically Applied Chemicals in Six Mammalian Species, Including Man: An In Vitro Study With Benzo(a)pyrene and Testosterone*. *Toxicol. Appl. Pharmacol.* 81:502-518.

Sanders, C.L., Skinner, C. and Gelman, R.H. (1986) *Percutaneous Absorption of 7,10 ¹⁴C-Benzo[a]pyrene and 7,12 ¹⁴C-Dimethylbenz[a]anthracene in Mice.* JEPTO 2:25-34.

Wester, R.C., Maibach, H.I., Bucks, D.A.W., Sedik, L., Melendres, J., Liao, C. and DiZio, S. (1990) *Percutaneous Absorption of [¹⁴C]DDT and [¹⁴C]Benzo[a]pyrene from Soil.* Fund. Appl. Toxicol. 15:510-516.

Yang, J.J., Roy, T.A. and Mackerer, C.R. (1986) *Percutaneous Absorption of Benzo[a]pyrene in the Rat: Comparison of In Vivo and In Vitro Results.* Toxicol. Ind. Health 2:409-416.

Yang, J.J., Roy, T.A., Krueger, A.J., Neil, W. and Mackerer, C.R. (1989) *In Vitro and In Vivo Percutaneous Absorption of Benzo[a]pyrene From Petroleum Crude-Fortified Soil in the Rat.* Bull. Environ. Contam. Toxicol. 43:207-214.

The dermal penetration of B[a]P, applied as a complex organic mixture, seems to be representative of the dermal penetration of other PAHs examined in this study (Dankovic et al., 1989) including pyrene, benzanthracene, benzofluorene, methylchrysene, chrysene, benzofluoranthene and benzo[e]pyrene. The dissapperance half-life of B[a]P was 6.7 hours with the other PAHs ranging from 5.0 - 8.8 hours. The dissappearance half-life of B[a]P was decreased to 3 hours when pure B[a]P was applied to skin in acetone. These data suggest a 50% decrease in dermal absorption of B[a]P when applied as an environmental mixture (20%) rather than as neat compound (40%). This compares closely with the upper limit of 18% dermal absorption efficiency selected from the study of Wester et al.(1990) for soil-associated B[a]P.

Dankovic, D.A., Wright, C.W., Zangar, R.C. and Springer, D.L. (1989) *Complex Mixture Effects on the Dermal Absorption of Benzo(a)pyrene and Other Polycyclic Aromatic Hydrocarbons From Mouse Skin.* J. Appl. Toxicol. 9:39-44.

The oral and dermal cancer potency value for benzo[a]pyrene is based on a dietary study in mice. In this study, an applied dose was used.

BENZO[a]PYRENE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
0.91 ———— = 1 0.91	0.18 ———— = 0.2 0.91	0.91 ———— = 1 0.91	0.91 ———— = 1 0.91

The oral and dermal chronic reference dose for benzo[a]pyrene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used. The chronic inhalation reference concentration for benzo[a]pyrene is based on a naphthalene inhalation study in humans. In this study, an applied dose was used.

BENZO[a]PYRENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

The oral and dermal subchronic reference dose for benzo[a]pyrene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used. The subchronic inhalation reference concentration for benzo[a]pyrene is based on a naphthalene inhalation study in humans. In this study, an applied dose was used.

BENZO[a]PYRENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

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BENZO[b]FLUORANTHENE

CAS #: 205992

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose: 0.04 mg/kg/day (2b)****Chronic Oral Reference Dose: 0.04 mg/kg/day (2f)****Subchronic Inhalation Reference Concentration: Not Volatile****Chronic Inhalation Reference Concentration: Not Volatile****Oral Cancer Potency Factor: $7.3 \text{ (mg/kg/day)}^{-1}$ (1g)****Inhalation Cancer Unit Risk: Not Volatile**

No specific quantitative information found on any route of exposure. Assume same as B[a]P.

The oral and dermal cancer potency value for benzo[b]fluoranthene is based on a dietary study in which B[a]P was administered to mice. In this study, an applied dose was used.

BENZO[b]FLUORANTHENE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

The oral and dermal chronic reference dose for benzo[b]fluoranthene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

BENZO[b]FLUORANTHENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

The oral and dermal subchronic reference dose for benzo[b]fluoranthene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

BENZO[b]FLUORANTHENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

BENZO[g,h,i]PERYLENE

CAS #: 191242

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose: 0.04 mg/kg/day (2b)****Chronic Oral Reference Dose: 0.04 mg/kg/day (2f)****Subchronic Inhalation Reference Concentration: Not Volatile****Chronic Inhalation Reference Concentration: Not Volatile****Oral Cancer Potency Factor: NC****Inhalation Cancer Unit Risk: Not Volatile**

No specific quantitative information found on any route of exposure. Assume same as B[a]P.

The oral and dermal chronic reference dose for benzo[g,h,i]perylene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

BENZO[g,h,i]PERYLENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

The oral and dermal subchronic reference dose for benzo[g,h,i]perylene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

BENZO[g,h,i]PERYLENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

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BENZO[k]FLUORANTHENE

CAS #: 207089

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose: 0.04 mg/kg/day (2b)****Chronic Oral Reference Dose: 0.04 mg/kg/day (2f)****Subchronic Inhalation Reference Concentration: Not Volatile****Chronic Inhalation Reference Concentration: Not Volatile****Oral Cancer Potency Factor: $7.3 \text{ (mg/kg/day)}^{-1}$ (1g)****Inhalation Cancer Unit Risk: Not Volatile**

No specific quantitative information found on any route of exposure. Assume same as B[a]P.

The oral and dermal cancer potency value for benzo[k]fluoranthene is based on a dietary study in which B[a]P was administered to mice. In this study, an applied dose was used.

BENZO[k]FLUORANTHENE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

The oral and dermal chronic reference dose for benzo[k]fluoranthene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

BENZO[k]FLUORANTHENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

The oral and dermal subchronic reference dose for benzo[k]fluoranthene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

BENZO[k]FLUORANTHENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose: 0.02 mg/kg/day (2)****Chronic Oral Reference Dose: 0.02 mg/kg/day (1)****Subchronic Inhalation Reference Concentration: Not Volatile****Chronic Inhalation Reference Concentration: Not Volatile****Oral Cancer Potency Factor: $0.014 \text{ (mg/kg/day)}^{-1}$ (1)****Inhalation Cancer Unit Risk: Not Volatile**

¹⁴C-DEHP appears to be efficiently absorbed from the gastrointestinal tract of the rat (Williams and Blanchfield, 1974). More than 90% of the radiolabel was excreted in urine. Fecal excretion was not quantified, suggesting oral absorption is probably close to 100%. A second study (Chadwick et al., 1982) demonstrated virtually complete absorption of ¹⁴C-DEHP administered in the diet to F344 rats.

Chadwick, M., Branfman, A.K. and Silveira, D.M. (1982) Dose-Dependence of and Effect of Prior Exposure on the Metabolism of DEHP Administered in the Diet to Rats. Report to Chemical Manufacturers Association. Arthur D. Little, Inc.

Williams, D.T. and Blanchfield, B.J. (1974) *Retention, Excretion and Metabolism of DEHP Administered Orally to the Rat.* Bull. Environ. Contam. Toxicol. 11:371-387.

DEHP appears to be poorly absorbed through skin (Elsisi et al., 1985). Only 7% of an occluded applied dose of ¹⁴C-DEHP was absorbed through shaved rat skin, as evidenced by the appearance of radiolabel in urine, feces and tissues. In a semi-occluded study (Elsisi et al., 1989), the shaved skin of F344 rats was exposed to ¹⁴C-phthalates in ethanol and covered with a perforated plastic cap. Radioactivity was monitored in urine and feces as an index of excretion. Bis(2-ethylhexyl)phthalate was poorly absorbed with less than 2% of the applied dose recovered in biological material (98% recovered at the site of application). The value of 2% is selected as the most appropriate since the experimental protocol most closely represents the human exposure scenario.

Elsisi, A. E., Carter, D. E. and Sipes, I. G. (1975). *Dermal Absorption and Tissue Distribution of Phthalate Esters.* Toxicologist. 5:246.

Elsisi, E., Carter, D.E. and Sipes, I.G. (1989) *Dermal Absorption of Phthalate Diesters in Rats.* Fund. Appl. Toxicol. 12:70-77.

The oral and dermal cancer potency value for bis(2-ethylhexyl)phthalate is based on an oral feeding (dietary) study in mice. The toxicity value is based on an applied dose.

DEHP RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.02}{1} = 0.02$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal chronic reference doses for DEHP is based on an oral feeding (dietary) study in guinea pigs. In this study, an applied dose was used.

DEHP RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.02}{1} = 0.02$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference doses for DEHP is based on an oral feeding (dietary) study in guinea pigs. In this study, an applied dose was used.

DEHP RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.02}{1} = 0.02$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.001 mg/kg/day (2e)

Chronic Oral Reference Dose: 0.001 mg/kg/day (2d)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: Not Volatile

Human studies have measured the oral absorption efficiency of cadmium compounds with a reported range of 1% - 7% (McLellan et al., 1978; Shaikh and Smith, 1980). The range of reported oral absorption efficiencies in experimental animals is lower than in humans, from 0.5% - 3% (Engstrom and Nordberg, 1979; Moore et al., 1973; Friberg et al., 1974). Higher doses tend to be absorbed less efficiently as do doses administered in food or milk, when compared to aqueous doses. Iron deficiency has been observed to increase the oral absorption of cadmium in humans and animals (ATSDR, 1989). Therefore, the upper-bounds of 7% (humans) and 3% (animals) are selected as protective estimates.

Agency for Toxic Substances and Disease Registry (ATSDR) (1989) Toxicological Profile for Cadmium. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service, pp. 46-49.

Engstrom, B. and Nordberg, G.F. (1979) *Dose-Dependence of Gastrointestinal Absorption and Biological Half-Time of Cadmium in Mice*. *Toxicology* 13:215-222.

Friberg, L., Piscator, M., Nordberg, G.F. and Kjellstrom, T. (1974) Cadmium in the Environment. 2nd ed. Boca Raton, FL: CRC Press.

McLellan, J.S., Flanagan, P.R., Chamberlain, M.J. and Valberg, L.S. (1978) *Measurement of Dietary Cadmium Absorption in Humans*. *J. Toxicol. Environ. Health* 4:131-138.

Moore, W., Stara, J.F., Crocker, W.C., Malanchuk, M. and Iltis, R. (1973) *Comparison of ¹¹⁵Cd Retention in Rats Following Different Routes of Administration*. *Environ. Res.* 6:473-478.

Shaikh, Z.A. and Smith, J.C. (1980) *Metabolism of Orally Ingested Cadmium in Humans*. In: Holmstedt, B. et al., eds. Mechanisms of Toxicity and Hazard Evaluation. Amsterdam: Elsevier/North-Holland, pp. 569-574.

Cadmium is poorly absorbed by the dermal route (ATSDR, 1989). An upper-bound estimate of 1% is probably appropriate and protective for human exposure (see chromium).

Agency for Toxic Substances and Disease Registry (ATSDR) (1989) Toxicological Profile for Cadmium. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service, pp. 46-49.

The oral and dermal chronic reference dose for cadmium is based on an oral dietary study in humans. In this study, an applied dose was used. The chronic inhalation reference concentration for cadmium is based on an inhalation study in humans. In this study, an applied dose was used.

CADMIUM RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.07}{0.07} = 1$	$\frac{0.01}{0.07} = 0.14$	$\frac{0.07}{0.07} = 1$	$\frac{0.07}{0.07} = 1$

The oral and dermal subchronic reference dose for cadmium is based on an oral dietary study in humans. In this study, as applied does was used.

CADMIUM RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.07}{0.07} = 1$	$\frac{0.01}{0.07} = 0.14$	$\frac{0.07}{0.07} = 1$	$\frac{0.07}{0.07} = 1$

CARBON TETRACHLORIDE

CAS #: 56235

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.007 mg/kg/day (2)

Chronic Oral Reference Dose: 0.0007 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: 430 $\mu\text{g}/\text{m}^3$ (3a)

Chronic Inhalation Reference Concentration: 430 $\mu\text{g}/\text{m}^3$ (3)

Oral Cancer Potency Factor: 0.13 (mg/kg/day)⁻¹ (1)

Inhalation Cancer Unit Risk: 0.000015 ($\mu\text{g}/\text{m}^3$)⁻¹ (1)

The oral absorption efficiency in animals is extensive. Studies have reported that 80-85% of an administered dose is recovered in expired air (Marchand et al., 1970; Paul and Rubinstein, 1963). This indicates that GI absorption is probably close to 100% since CCl_4 is metabolized with metabolites appearing in urine and feces.

Marchand, C., McLean, S. and Plaa, G.L. (1970) *The Effect of SKF525A on the Distribution of Carbon Tetrachloride in Rats.* J. Pharmacol. Exp. Therap. 714:232-238.

Paul, B.B. and Rubenstein, D. (1963) *Metabolism of Carbon Tetrachloride and Chloroform by the Rat.* J. Pharmacol. Exp. Therap. 141:141-148.

No studies were located containing quantitative information on the dermal absorption efficiency of carbon tetrachloride. Assume that the dermal absorption is similar to that of other volatile organics such as benzene whose dermal absorption efficiency has been estimated to be 10% of a non-occluded applied dose in 24 hours.

The oral and dermal cancer potency value for carbon tetrachloride is based on a gavage study in rodents. This toxicity value is based on applied dose.

CARBON TETRACHLORIDE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal chronic reference dose for carbon tetrachloride is based on an oral gavage study (via corn oil) in rats. In this study, an applied dose was used.

CARBON TETRACHLORIDE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for carbon tetrachloride is based on an oral gavage study (via corn oil) in rats. In this study, an applied dose was used.

CARBON TETRACHLORIDE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

CHLOROBENZENE

CAS#: 108907

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.2 mg/kg/day (2)

Chronic Oral Reference Dose: 0.02 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: 200 $\mu\text{g}/\text{m}^3$ (2)

Chronic Inhalation Reference Concentration: 20 $\mu\text{g}/\text{m}^3$ (2)

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: NC

The oral absorption efficiency of chlorobenzene has been reported to range from at least 18% in rats to at least 31% in humans (Lindsay-Smith et al., 1972; Ogata and Shimada, 1983). These estimates are probably low since the studies failed to quantitate exhaled compounds. A more conservative estimate may be 100%, based on its structural similarity to benzene.

Lindsay-Smith, J.R., Shaw, B.A.J. and Foulkes, D.M. (1972) *Mechanisms of Mammalian Hydroxylation: Some Novel Metabolites of Chlorobenzene*. *Xenobiotics* 2:215-226.

Ogata, M. and Shimada, Y. (1983) *Differences in Urinary Monochlorobenzene Metabolites Between Rats and Humans*. *Int. Arch. Occup. Environ. Health* 53:51-57.

No studies were located regarding the dermal absorption of chlorobenzene. Assume it to be similar to benzene (10% non-occluded, 24 hours).

The oral and dermal chronic reference dose for chlorobenzene is based on an oral (capsule) study in dogs. In this study, an applied dose was used.

CHLOROBENZENE Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for chlorobenzene is based on an oral (capsule) study in dogs. In this study, an applied dose was used.

CHLOROBENZENE Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

CHLOROFORM

CAS#: 67663

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.01 mg/kg/day (2)

Chronic Oral Reference Dose: 0.01 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: 660 $\mu\text{g}/\text{m}^3$ (3a)

Chronic Inhalation Reference Concentration: 660 $\mu\text{g}/\text{m}^3$ (3)

Oral Cancer Potency Factor: 0.0061 (mg/kg/day)⁻¹ (1)

Inhalation Cancer Unit Risk: 0.000023 ($\mu\text{g}/\text{m}^3$)⁻¹ (1)

Oral absorption efficiency of chloroform in humans and animals is essentially 100% (Fry et al., 1972; Brown et al., 1974; Taylor et al., 1974).

Brown, D.M., Langley, P.F., Smith, D. and Taylor, D.C. (1974) *Metabolism of Chloroform. I. The Metabolism of ¹⁴C-Chloroform by Different Species.* *Xenobiotica.* 4:151-163.

Fry, B.J., Taylor, T. and Hathaway, D.E. (1972) *Pulmonary Elimination of Chloroform and its Metabolites in Man.* *Arch. Int. Pharmacodyn.* 196:98-11.

Taylor, D.C., Brown, D.M., Kuble, R. and Langley, P.F. (1974) *Metabolism of Chloroform. II. A Sex Difference in the Metabolism of ¹⁴C-Chloroform in Mice.* *Xenobiotica.* 4:165-174.

Dermal absorption of chloroform is rapid and quite large (329 $\mu\text{mol}/\text{min}/\text{cm}^2$) across mouse skin (Tsurata, 1975). This suggests that an occluded dose would be 100% absorbed with a non-occluded dose being absorbed less efficiently (perhaps 10% as with benzene) due to rapid volatilization.

Tsurata, H. (1975) *Percutaneous Absorption of Organic Solvents. I. Comparative Study of the in Vivo Percutaneous Absorption of Chlorinated Solvents in Mice.* *Ind. Health.* 13:227-236.

The oral and dermal cancer potency value for chloroform is based on an oral drinking water study in rats. This toxicity value is not based on absorbed dose.

CHLOROFORM RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal chronic reference dose for chloroform is based on an oral (toothpaste) study conducted in dogs. In this study, an applied dose was used.

CHLOROFORM RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for chloroform is based on an oral (toothpaste) study conducted in dogs. In this study, an applied dose was used.

CHLOROFORM RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.02 mg/kg/day (2g)

Chronic Oral Reference Dose: 0.005 mg/kg/day (1d)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: Not Volatile

Oral absorption in humans ranges from 0.4% (chromium III) to 11% (chromium VI) (Donaldson and Barreras, 1966; Anderson et al., 1983). Animal studies (Mertz et al., 1965; Donaldson and Barreras, 1966; Ogawa, 1976) indicate the same range of oral absorption (1.4% for chromium III - 11% for chromium VI). The upper limit of 11% will be used as an estimate of the oral absorption efficiency of chromium in humans and experimental animals.

Anderson, R.A., Polansky, M.M., Bryden, N.A., Patterson, K.Y., Veillon, C. and Glinsmann, W.H. (1983) *Effects of Chromium Supplementation on Urinary Cr Excretion of Human Subjects and Correlation of Cr Excretion with Selected Clinical Parameters*. J. Nutr. 113:276-281.

Donaldson, R.M. and Barreras, R.F. (1966) *Intestinal Absorption of Trace Quantities of Chromium*. J. Lab. Clin. Med. 68:484-493.

Mertz, W., Roginski, E.E. and Reba, R.C. (1965) *Biological Activity and Fate of Trace Quantities of Intravenous Chromium(III) in the Rat*. Am. J. Physiol. 209:489-494.

Ogawa, E. (1976) *Experimental Study on Absorption, Distribution and Excretion of Trivalent and Hexavalent Chromes*. Jap. J. Pharmacol. 26:92-103.

Chromium can be absorbed through the intact skin of humans and animals, however, no studies were located which quantitatively described the rate or extent of dermal absorption. A dermal absorption efficiency of 1% for chromium contaminated soils has been used (Sheehan et al., 1991) based on EP toxicity tests. In these tests, less than 1% of soil-adsorbed chromium was extracted with Ph 5 solution over 24 hours. These conditions are more conducive to extraction than dermal conditions. Therefore, this 1% figure is taken as a conservative upper-bound estimate of dermal bioavailability.

Sheehan, P.J., Meyers, D.M., Sauer, M.M. and Paustenbach, D.J. (1991) *Assessment of the Human Health Risks Posed by Exposure to Chromium-Contaminated Soils*. J. Toxicol. Environ. Health 32:161-201.

The oral and dermal chronic reference dose for chromium is based on a drinking water ingestion study conducted in animals. In this study, an applied dose was used.

CHROMIUM RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.11}{0.11} = 1$	$\frac{0.01}{0.11} = 0.09$	$\frac{0.11}{0.11} = 1$	$\frac{0.11}{0.11} = 1$

The oral and dermal subchronic reference dose for chromium is based on a drinking water ingestion study conducted in animals. In this study, an applied dose was used.

CHROMIUM RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.11}{0.11} = 1$	$\frac{0.01}{0.11} = 0.09$	$\frac{0.11}{0.11} = 1$	$\frac{0.11}{0.11} = 1$

CHRYSENE

CAS #: 218019

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose:** 0.04 mg/kg/day (2b)**Chronic Oral Reference Dose:** 0.04 mg/kg/day (2f)**Subchronic Inhalation Reference Concentration:** Not Volatile**Chronic Inhalation Reference Concentration:** Not Volatile**Oral Cancer Potency Factor:** $7.3 \text{ (mg/kg/day)}^{-1}$ (1g)**Inhalation Cancer Unit Risk:** Not Volatile

No specific quantitative information found on the absorption via the oral or dermal route.
Assume same as B[a]P.

The oral and dermal cancer potency value for chrysene is based on a dietary study in which B[a]P was administered to mice. In this study, an applied dose was used.

CHRYSENE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

The oral and dermal chronic reference dose for chrysene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

CHRYSENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

The oral and dermal subchronic reference dose for chrysene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

CHRYSENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.02 mg/kg/day (2)

Chronic Oral Reference Dose: 0.02 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: 1 $\mu\text{g}/\text{m}^3$ (4)

Chronic Inhalation Reference Concentration: 7 $\mu\text{g}/\text{m}^3$ (4)

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: NC

The oral absorption efficiency of cyanide is difficult to quantitate from the few existing studies. In dogs, the absorption of cyanide (KCN) was estimated to be between 17% and 72%, with smaller doses being absorbed more efficiently (Gettler and Baine, 1938). However, the animals died shortly after dosing which most likely limited the absorptive phase. In a human suicide attempt (Liebowitz and Schwartz, 1948), a very speculative absorption efficiency of 78% was calculated based on blood levels and estimation of the ingested dose. Both estimates may underestimate the actual absorption efficiency. Therefore, 100% is assumed to be a more representative oral absorption efficiency.

Gettler, A.O. and Baine, J.O. (1938) *The Toxicology of Cyanide*. Am. J. Med. Sci. 195:182-198.

Liebowitz, D. and Schwartz, H. (198) *Cyanide Poisoning*. Am. J. Clin. Pathol. 18:965-970.

No studies were located to quantitate the dermal absorption efficiency of cyanides. Available evidence suggests that dermal absorption does occur and may be quite extensive in some situations (ATSDR, 1989). Assume the dermal absorption to be similar to arsenic which was estimated at 3% based on EP toxicity studies.

Agency for Toxic Substances and Disease Registry (ATSDR) (1989) Toxicological Profile for Cyanide. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service, pp. 36-38.

The oral and dermal chronic reference dose for cyanide is based on an oral feeding (dietary) study conducted in rats. In this study, an applied dose was used.

CYANIDE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.03}{1} = 0.03$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for cyanide is based on an oral feeding (dietary) study conducted in rats. In this study, an applied dose was used.

CYANIDE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.03}{1} = 0.03$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

DIBENZO[a,h]ANTHRACENE

CAS #: 53703

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.04 mg/kg/day (2b)

Chronic Oral Reference Dose: 0.04 mg/kg/day (2f)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: $7.3 \text{ (mg/kg/day)}^{-1}$ (1g)

Inhalation Cancer Unit Risk: Not Volatile

No specific quantitative information found on the oral route. Assume same as B[a]P.

Dermal absorption has been documented to occur less efficiently than B[a]P. 33% of a dermal dose was estimated to have been absorbed after 24 hours from shaved mouse skin compared to 83% absorption for B[a]P under similar conditions (Sanders et al., 1986). This converts to 16% absorption of an applied dermal dose of neat compound or 8% absorption of an applied dermal dose of a complex environmental mixture.

Sanders, C.L., Skinner, C. and Gelman, R.A. (1986) *Percutaneous Absorption of 7,10 ¹⁴C-Benzo[a]pyrene and 7,12 ¹⁴C-Dimethylbenzo[a]pyrene in Mice.* JEPTO. 7:25-34.

The oral and dermal cancer potency value for dibenzo[a,h]anthracene is based on a dietary study in which B[a]P was administered to mice. In this study, an applied dose was used.

DIBENZO[a,h]ANTHRACENE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.08}{0.91} = 0.09$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

The oral and dermal chronic reference dose for dibenzo[a,h]anthracene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

DIBENZO[a,h]ANTHRACENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.08}{1} = 0.08$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

The oral and dermal subchronic reference dose for dibenzo[a,h]anthracene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

DIBENZO[a,h]ANTHRACENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.08}{1} = 0.08$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

1,1-DICHLOROETHANE

CAS #: 75343

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 1 mg/kg/day (2)

Chronic Oral Reference Dose: 0.1 mg/kg/day (2)

Subchronic Inhalation Reference Concentration: 5000 $\mu\text{g}/\text{m}^3$ (2)

Chronic Inhalation Reference Concentration: 500 $\mu\text{g}/\text{m}^3$ (2)

Oral Cancer Potency Factor: Not Quantified

Inhalation Cancer Unit Risk: Not Quantified

No specific studies were located quantifying the respiratory absorption efficiency of 1,1-dichloroethane. The blood/air partitioning coefficient of 1,1-dichloroethane is approximately 4 times less than that of 1,2-dichloroethane suggesting less efficient pulmonary absorption of 1,1-dichloroethane than 1,2-dichloroethane. However, assume the 75% inhalation efficiency of 1,2-dichloroethylene is applicable.

No specific studies were located quantifying the oral absorption efficiency of 1,1-dichloroethane. Assume it to be the same as 1,2-dichloroethane (100%).

No specific studies were located quantifying the dermal absorption efficiency of 1,1-dichloroethane. Assume it to be similar to that of other volatile compounds (benzene) whose dermal absorption efficiency may reach 10% of a non-occluded applied dose in 24 hours.

The oral and dermal chronic reference dose for 1,1-dichloroethane is based on an inhalation study conducted in rats. In this study, an applied dose was used.

1,1-DCA RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{0.75} = 1.3$	$\frac{0.1}{0.75} = 0.13$	$\frac{1}{0.75} = 1.3$	$\frac{1}{0.75} = 1.3$

The oral and dermal subchronic reference dose for 1,1-dichloroethane is based on an inhalation study conducted in rats. In this study, an applied dose was used.

1,1-DCA RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{0.75} = 1.3$	$\frac{0.1}{0.75} = 0.13$	$\frac{1}{0.75} = 1.3$	$\frac{1}{0.75} = 1.3$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.2 mg/kg/day (4)

Chronic Oral Reference Dose: 0.02 mg/kg/day (4)

Subchronic Inhalation Reference Concentration: 55 $\mu\text{g}/\text{m}^3$ (3a)Chronic Inhalation Reference Concentration: 55 $\mu\text{g}/\text{m}^3$ (3)Oral Cancer Potency Factor: 0.091 (mg/kg/day)⁻¹ (2)Inhalation Cancer Unit Risk: 0.000026 ($\mu\text{g}/\text{m}^3$)⁻¹ (2)

Studies in experimental animals indicate that the oral absorption of 1,2-dichloroethane is rapid and complete. Reitz et al. (1980) reported complete recovery of an oral dose of ¹⁴C-1,2-dichloroethane in the urine, carcass and expired air, suggesting 100% absorption. Comparison of blood levels attained following intravenous and oral dosing also supports the belief that oral absorption is 100% (Spreafico et al., 1980).

Reitz, R.H., Fox, T.R. and Domoradzski, J.Y. (1980) *Pharmacokinetics and Macromolecular Interactions of Ethylene Dichloride: Comparison of Oral and Inhalation Exposures*. In: Ames, B.N., Infante, P. and Reitz, R. eds. Ethylene Dichloride: A Potential Health Risk? Cold Spring Harbor, NY: Cold Spring Harbor Laboratory, pp. 135-148.

Spreafico, K., Zuccato, E. and Marcucci, F. (1980) *Pharmacokinetics of Ethylene Dichloride in Rats Treated by Different Routes and its Long-term Inhalatory Toxicity*. In: Ames, B.N., Infante, P. and Reitz, R. eds. Ethylene Dichloride: A Potential Health Risk? Cold Spring Harbor, NY: Cold Spring Harbor Laboratory, pp. 107-133.

No specific information was found to quantify the dermal absorption efficiency of 1,2-dichloroethane. Assume it to be similar to other volatile compounds (benzene) which may reach 10% of a non-occluded applied dose in 24 hours.

The oral and dermal cancer potency value for 1,2-dichloroethane is based on a gavage study in rats. This toxicity value is not based on absorbed dose.

1,2-DCA RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal chronic reference dose for 1,2-dichloroethane is based on an inhalation study conducted in rats. An absorption efficiency of 30% was used to calculate an absorbed dose. The RAFs for all pathways are therefore the absorption efficiency of 1,2-dichloroethane by the route in question.

1,2-DCA RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.1	1	1

The oral and dermal subchronic reference dose for 1,2-dichloroethane is based on an inhalation study conducted in rats. An absorption efficiency of 30% was used to calculate an absorbed dose. The RAFs for all pathways are therefore the absorption efficiency of 1,2-dichloroethane by the route in question.

1,2-DCA RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.1	1	1

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose: 0.009 mg/kg/day (2)****Chronic Oral Reference Dose: 0.009 mg/kg/day (1)****Subchronic Inhalation Reference Concentration: 5 $\mu\text{g}/\text{m}^3$ (3a)****Chronic Inhalation Reference Concentration: 5 $\mu\text{g}/\text{m}^3$ (3)****Oral Cancer Potency Factor: 0.6 (mg/kg/day)⁻¹ (1)****Inhalation Cancer Unit Risk: 0.00005 ($\mu\text{g}/\text{m}^3$)⁻¹ (1)**

Since 1,1-dichloroethylene is a small organic molecule with chemical and physical properties similar to the lipid soluble anaesthetics, it is expected to penetrate the pulmonary epithelium rapidly and efficiently. An inhalation absorption efficiency of 98% is derived from metabolic excretion data of inhaled radiolabeled 1,1-dichloroethylene data in the rat (McKenna et al., 1977).

McKenna, M.J., Watanabe, P.G. and Gehring, P.J. (1977) *Pharmacokinetics of Vinylidene Chloride in the Rat*. *Environ. Health Perspect.* 21:99-105.

The oral absorption of 1,1-dichloroethylene in animals has been demonstrated to be rapid and essentially complete (100%). (Reichert et al., 1979; Jones and Hathaway, 1978; McKenna et al., 1978; Putcha et al., 1986).

McKenna, M.J., Zemple, J.A., Madrid, E.O., Braun, W.H. and Gehring, P.J. (1978) *Metabolism and Pharmacokinetic Profile of Vinylidene Chloride in Rats Following Oral Administration*. *Toxicol. Appl. Pharmacol.* 45:821-835.

Reichert, D., Werner, H.E. and Metzler, M. (1979) *Molecular Mechanism of 1,1-Dichloroethylene Toxicity: Excreted Metabolites Reveal Different Pathways of Reactive Intermediates*. *Arch. Toxicol.* 42:159-169.

Jones, P.K. and Hathaway, D.E. (1978) *Differences in Metabolism of Vinylidene Chloride Between Mice and Rats*. *Br. J. Cancer.* 37:411-417.

Putcha, L., Bruchner, J.V. and D'Soyza, R. (1986) *Toxicokinetics and Bioavailability of Oral and Intravenous 1,1-Dichloroethylene*. *Fund. Appl. Toxicol.* 6:240-250.

No studies were located regarding the dermal absorption of 1,1-dichloroethylene. Due to its chemical and physical properties, dermal absorption is expected to be 100% of an occluded applied dose or 10% of a non-occluded applied dose (same as benzene).

The oral and dermal cancer potency estimate for 1,1-dichloroethylene is based on an inhalation study in rats. In this study, an applied dose was used.

1,1-DCE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{0.98} = 1.02$	$\frac{0.1}{0.98} = 0.102$	$\frac{1}{0.98} = 1.02$	$\frac{1}{0.98} = 1.02$

The oral and dermal chronic reference dose for 1,1-dichloroethylene is based on a chronic oral drinking water study conducted in rats. In this study, an applied dose was used.

1,1-DCE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for 1,1-dichloroethylene is based on a chronic oral drinking water study conducted in rats. In this study, an applied dose was used.

1,1-DCE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

1,2-DICHLOROETHYLENE

CAS #: 156605

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose:** 0.2 mg/kg/day (2)**Chronic Oral Reference Dose:** 0.02 mg/kg/day (1)**Subchronic Inhalation Reference Concentration:** 1100 $\mu\text{g}/\text{m}^3$ (3a)**Chronic Inhalation Reference Concentration:** 1100 $\mu\text{g}/\text{m}^3$ (3)**Oral Cancer Potency Factor:** NC**Inhalation Cancer Unit Risk:** NC

No studies were located addressing the oral or dermal absorption efficiency of 1,2-dichloroethylene. Assume behavior similar to 1,1-dichloroethylene and benzene (100% oral and 10% non-occluded dermal absorption efficiencies).

The oral and dermal chronic reference dose for 1,2-dichloroethylene is based on an oral drinking water study conducted in mice. In this study, an applied dose was used.

1,2-DCE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for 1,2-dichloroethylene is based on an oral drinking water study conducted in mice. In this study, an applied dose was used.

1,2-DCE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

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TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 1 mg/kg/day (2)

Chronic Oral Reference Dose: 0.1 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: 1000 $\mu\text{g}/\text{m}^3$ (2)

Chronic Inhalation Reference Concentration: 1000 $\mu\text{g}/\text{m}^3$ (1)

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: NC

Animal studies indicate that ethylbenzene is quickly and efficiently absorbed by the oral route. Estimates range from 72%-92% in one study (El Masry et al., 1956) to 84% in a second study (Climie et al., 1983). A value of 100% is selected since these studies underestimated oral absorption by not controlling for respiratory volatilization following oral absorption.

Climie, I.J.G., Hutson, D.H. and Stoydin, G. (1983) *The Metabolism of Ethylbenzene Hydroperoxide in the Rat*. *Xenobiotica* 13:611-618.

El Masry, A.M., Smith, J.N. and Williams, R.T. (1956) *The Metabolism of Alkylbenzenes: n-Propylbenzene and n-Butylbenzene with Further Observations on Ethylbenzene*. *Biochem. J.* 64:50-56.

Absorption of pure liquid ethylbenzene and aqueous solutions containing ethylbenzene through human skin is rapid and substantial (20-30 $\text{mg}/\text{cm}^2/\text{hr}$) (Gromiec and Piotrowski, 1984). Occluded doses could potentially be 100% absorbed. The non-occluded dermal absorption of ethylbenzene has been measured to be 3.4% of an applied dose in 4 hours (Susten et al., 1990). This calculates to a 24 hour dermal absorption efficiency of 20%.

Susten, A.S., Niemeier, R.W. and Simon, S.D. (1990) *In Vivo Percutaneous Absorption Studies of Volatile Organic Solvents in Hairless Mice II. Toluene, Ethylbenzene and Aniline*. *J. Appl. Toxicol.* 10:217-225.

Gromiec, J.P. and Piotrowski, J.K. (1984). *Urinary Mandelic Acid as an Exposure Test for Ethylbenzene*. *Int. Arch. Occup. Environ. Health* 55:61-72.

The oral and dermal chronic reference dose for ethylbenzene is based on an oral gavage (via olive oil) study conducted in rats. In this study, an applied dose was used.

ETHYLBENZENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.2}{1} = 0.2$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for ethylbenzene is based on an oral gavage (via olive oil) study conducted in animals. In this study, an applied dose was used.

ETHYLBENZENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.2}{1} = 0.2$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.0002 mg/kg/day (4)

Chronic Oral Reference Dose: 0.00002 mg/kg/day (4)

Subchronic Inhalation Reference Concentration: 1.2 $\mu\text{g}/\text{m}^3$ (4)Chronic Inhalation Reference Concentration: 0.2 $\mu\text{g}/\text{m}^3$ (4)Oral Cancer Potency Factor: 85 (mg/kg/day)⁻¹ (1)Inhalation Cancer Unit Risk: 0.00022 ($\mu\text{g}/\text{m}^3$)⁻¹ (1)

Using ¹⁴C-1,2-dibromoethane, the oral absorption efficiency of ethylene dibromide was estimated to be at least 75% based on excretion of radiolabel in urine and feces (Plotnick et al., 1979). This study failed to quantitate radiolabel in expired air, therefore, absorption is assumed to be 100% by the oral route.

Plotnick, H.B., Weigel, W.W. and Richards, D.E. (1979) *The Effect of Dietary Disulfiram Upon the Tissue Distribution and Excretion of ¹⁴C-1,2-Dibromoethane in the Rat*. Res. Commun. Chem. Pathol. Pharmacol. 26:535-543.

No studies exist quantitating the dermal absorption of EDB. However, based on its chemical and physical properties, it is highly likely that 100% of an occluded dermal dose would be absorbed and 10% of a non-occluded dermal applied dose.

The oral and dermal cancer potency value for ethylene dibromide is based on a gavage study in rats. This toxicity value is not based on absorbed dose.

ETHYLENE DIBROMIDE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal chronic reference dose is based on an oral feeding study in bulls. In this study, an applied dose was used.

ETHYLENE DIBROMIDE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose is based on an oral feeding study in bulls. In this study, an applied dose was used.

ETHYLENE DIBROMIDE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.4 mg/kg/day (2)

Chronic Oral Reference Dose: 0.04 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: Not Volatile

No specific quantitative information found on the absorption via the oral or dermal route. Assume same as B[a]P.

The oral and dermal chronic reference dose for fluoranthene is based on an oral gavage study conducted in mice. In this study, an applied dose was used.

FLUORANTHENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

The oral and dermal subchronic reference dose for fluoranthene is based on an oral gavage study conducted in mice. In this study, an applied dose was used.

FLUORANTHENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

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TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.4 mg/kg/day (2)

Chronic Oral Reference Dose: 0.04 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: Not Volatile

No specific quantitative information found on the absorption via oral, inhalation or dermal route. Assume same as B[a]P.

The oral and dermal chronic reference dose for fluorene is based on an oral gavage study conducted in mice. In this study, an applied dose was used.

FLUORENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

The oral and dermal subchronic reference dose for fluorene is based on an oral gavage study conducted in mice. In this study, an applied dose was used.

FLUORENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

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TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.04 mg/kg/day (2b)

Chronic Oral Reference Dose: 0.04 mg/kg/day (2f)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: $7.3 \text{ (mg/kg/day)}^{-1}$ (1g)

Inhalation Cancer Unit Risk: Not Volatile

No specific quantitative information found on the absorption via oral, inhalation or dermal route. Assume same as B[a]P.

The oral and dermal cancer potency value for indeno[1,2,3-cd]pyrene is based on a dietary study in which B[a]P was administered to mice. In this study, an applied dose was used.

INDENO[1,2,3-cd]PYRENE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

The oral and dermal chronic reference dose for indeno[1,2,3-cd]pyrene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

INDENO[1,2,3-cd]PYRENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

The oral and dermal subchronic reference dose for indeno[1,2,3-cd]pyrene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

INDENO[1,2,3-cd]PYRENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.00075 mg/kg/day (4)

Chronic Oral Reference Dose: 0.00075 mg/kg/day (4)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: Not Quantified

Inhalation Cancer Unit Risk: Not Volatile

The oral absorption efficiency of lead compounds in adult experimental animals and adult humans ranges from 1% - 15% (EPA, 1986; Hammond, 1982; Chamberlain et al., 1978). Young humans and experimental animals absorb lead with higher efficiency, estimates ranging up to 50% (Hammond, 1982; Kostial et al., 1971, 1978; Forbes and Reina, 1972). The estimate of 50% is considered as being a conservative upper-bound for humans and experimental animals.

Chamberlain, A., Hard, C. and Little, M.J. (1978) Investigations into Lead from Motor Vehicles. Harwell, U.K.: United Kingdom Atomic Energy Authority. Rep. No. AERE-9198.

U.S. Environmental Protection Agency (EPA) (1986) Air Quality Criteria for Lead. June 1986 and Addendum, September, 1986. Research Triangle Park, NC: Office of Research and Development, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, EPA. EPA 600/8-83-018F.

Forbes, G.B. and Reina, J.C. (1972) *Effect of Age on Gastrointestinal Absorption (Fe, Sr, Pb) in the Rat*. J. Nutr. 102:647-652.

Hammond, P.B. (1982) *Metabolism of Lead*. In: Chisolm, J.J. and O'Hara, D.M., eds. Lead Absorption in Children: Management, Clinical and Environmental Aspects. Baltimore, MD: Urban and Schwarzenberg, pp. 11-20.

Kostial, K., Simonovic, J. and Pisonic, M. (1971) *Lead Absorption from the Intestine in Newborn Rats*. Nature 233:564-567.

The dermal absorption efficiency for lead as lead acetate has been reported to be 0.3% (12 hours) of an applied dose in humans, or 0.6% in 24 hours (Moore et al., 1980). Organic lead compounds are absorbed more rapidly and extensively than inorganic lead compounds.

Moore, M.R., Meredith, P.A., Watson, W.S., Sumner, D.J., Taylor, M.K. and Goldberg, A. (1980) *The Percutaneous Absorption of Lead-203 in Humans from Cosmetic Preparations Containing Lead Acetate, As Assessed by Whole-Body Counting and Other Techniques*. Food. Cosmet. Toxicol. 18:399-405.

The oral and dermal chronic reference dose for lead is based on back-calculation from the drinking water action level. In this calculation, an absorbed dose was used. Therefore, the RAF is the absorption efficiency by the route in question.

LEAD RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
0.5	0.006	0.5	0.5

The oral and dermal subchronic reference dose for lead is based on back-calculation from the drinking water action level. In this calculation, an absorbed dose was used. Therefore, the RAF is the absorption efficiency by the route in question.

LEAD RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
0.5	0.006	0.5	0.5

MERCURY

CAS #: 7439976

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.0003 mg/kg/day (2)

Chronic Oral Reference Dose: 0.0003 mg/kg/day (2)

Subchronic Inhalation Reference Concentration: 0.3 $\mu\text{g}/\text{m}^3$ (2)

Chronic Inhalation Reference Concentration: 0.3 $\mu\text{g}/\text{m}^3$ (2)

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: NC

MERCURY (elemental)

Oral absorption of metallic mercury has been estimated to be, at most, 0.10% (Friberg and Nordberg, 1973). The oral absorption efficiency of 0.01% in humans and laboratory animals is most frequently cited in the literature (Owen, 1990). The value of 0.1% is suggested as a conservative upper limit for human exposure.

Friberg, L., Nordberg, F. (1973) *Inorganic Mercury - A Toxicological and Epidemiological Appraisal*. In: Miller, M.W., Clarkson, T.W., ed. Mercury, Mercurials and Mercaptans. Springfield, Illinois: Charles C. Thomas, pp. 5-22.

Owen, B.A. (1990) *Literature-Derived Absorption Coefficients for 39 Chemicals Via Oral and Inhalation Routes of Exposure*. *Regul. Toxicol. Pharmacol.* 11:237-252.

Hursh et al. (1989) report maximum systemic mercury as a fraction of initial amounts of mercury on the skin. The average percentage absorbed (from data obtained from 5 human volunteers) can be calculated as 40% of the free mercury deposited on the skin. Assuming that 10% of the mercury in soil could be extracted and available for dermal absorption (Landa, 1978), a dermal absorption factor of 0.04 is obtained.

Hursh, J.B., Clarkson, T.W., Miles, E.F., et al. (1989) *Percutaneous Absorption of Mercury Vapor by Man*. *Arch. Environ. Health* 44:120-127.

Landa, E.R. (1978) *The Retention of Metallic Mercury Vapor by Soils*. *Geochem. Cosmochim. Acta*. 42:1407-1411.

MERCURY (inorganic)

An oral absorption efficiency of 15% is frequently cited in the literature (Owen, 1990). The range of values is 1% (mice) - 15% (humans) (Weiss et al., 1973; Clarkson, 1971), 15% being chosen as a protective estimate. Oral feeding of mercury-contaminated soil to mice (5% of diet) resulted in an oral absorption efficiency of 0.4% (Revis et al., 1990), compared to a 1% absorption efficiency for non-soil associated mercury. The form of mercury in the soil was 88% inorganic, 7% elemental and 0.01% organic. Since the soil-associated efficiency is approximately half the reported efficiency for non-soil associated mercury in mice, this suggests a protective human oral absorption efficiency of soil-adsorbed mercury of 7.5%.

Revis, N.W., Osborne, T.R., Holdsworth, G. and Hadden, C. (1990) *Mercury in Soil: A Method for Assessing Acceptable Limits*. *Arch. Environ. Contam. Toxicol.* 19:221-226.

Agency for Toxic Substances and Disease Registry (ATSDR) (1989) Toxicological Profile for Mercury, Agency for Toxic Substances and Disease Registry, U.S. Public Health Service, pp. 37-40.

Kostial, K., Kello, D., Jugo, S., et al. (1978) *Influence of Age on Metal Metabolism and Toxicity*. *Environ. Health Perspect.* 25:81-86.

Owen, B.A. (1990) *Literature-Derived Absorption Coefficients for 39 Chemicals Via Oral and Inhalation Routes of Exposure*. *Regul. Toxicol. Pharmacol.* 11:237-252.

Weiss, S.H., Wands, J.R., Yardley, J.H. (1973) *Demonstration by Electron Defraction of Black Mercury Sulfide (b-HgS) in a Case of "Melanosis coli and Black Kidneys" Caused by Chronic Inorganic Mercury Poisoning* [Abstract]. *Lab. Invest.* 5:401-402.

Clarkson, T.W. (1971) *Epidemiological and Experimental Aspects of Lead and Mercury Contamination*. *Food Cosmet. Toxicol.* 9:229-243.

Aqueous solutions of mercuric chloride applied to the skin of human volunteers were calculated to result in the absorption of 20 to 65 percent of the applied dose (Baranowska-Dutkiewicz, 1982). Assuming that 10% of the mercury in soil could be extracted and available for dermal absorption (Landa, 1978), a dermal absorption factor of 0.065 (6.5%) is obtained.

Baranowska-Dutkiewicz, B. (1982) *Evaluation of the Skin Uptake of Mercuric Chloride in Man*. *Journal of Applied Toxicology.* 2:223-225.

Landa, E.R. (1978) *The Retention of Metallic Mercury Vapor by Soils*. *Geochem. Cosmochim. Acta.* 42:1407-1411.

MERCURY (organic)

The oral absorption efficiency of methylmercury is reported as 95% (Aberg et al., 1969; Owen, 1990). Other forms of organic mercury may be orally absorbed less efficiently, with estimates ranging down to 80% (Fitzhugh et al., 1950).

Owen, B. A. (1990) *Literature-Derived Absorption Coefficients for 39 Chemicals Via Oral and Inhalation Routes of Exposure*. *Regul. Toxicol. Pharmacol.* 11:237-252.

Aberg, B., Elkman, R., Falk, U., et al. (1969) *Metabolism of Methylmercury (^{203}Hg) Compounds in Man: Excretion and Distribution*. *Arch. Environ. Health* 19:478-484.

Fitzhugh, O.G., Nelson, A.A., Laug, E.P., et al. (1950) *Chronic Oral Toxicities of Mercuri-phenyl and Mercuric Salts*. *Arch. Ind. Hyg. Occup. Med.* 2:433-442

Methyl mercury (in water) applied to the skin of guinea pigs at two dose levels resulted in 3.4% and 4.5% of the applied dose being absorbed (Skog and Wahlberg, 1964). Given the lipophilicity of organomercurials, an absorption value of 4.5% was chosen.

Skog, E. and Wahlberg, J.E. (1964) *A Comparative Investigation of the Percutaneous Absorption of Metal Compounds in the Guinea Pig by Means of the Radioactive Isotopes: ^{51}Cr , ^{58}Co , ^{65}Zn , $^{110\text{m}}\text{Ag}$, $^{115\text{m}}\text{Cd}$, ^{203}Hg* . *J. Invest. Dermatol.* 43:187-192.

The dermal and oral chronic reference dose for mercury is based on a human study of blood levels of methyl mercury. In this study, an administered (applied) dose was calculated from a blood level of 200 ng Hg/ml blood.

MERCURY RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.95}{0.95} = 1$	$\frac{0.045}{0.95} = 0.05$	$\frac{0.95}{0.95} = 1$	$\frac{0.95}{0.95} = 1$

The dermal and oral subchronic reference dose for mercury was adopted from the chronic oral RfD for methyl mercury, an estimated applied dose based upon blood levels of methyl mercury.

MERCURY RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.95}{0.95} = 1$	$\frac{0.045}{0.95} = 0.05$	$\frac{0.95}{0.95} = 1$	$\frac{0.95}{0.95} = 1$

METHYLENE CHLORIDE

CAS #: 75092

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.06 mg/kg/day (2)

Chronic Oral Reference Dose: 0.06 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: 3000 $\mu\text{g}/\text{m}^3$ (2)

Chronic Inhalation Reference Concentration: 3000 $\mu\text{g}/\text{m}^3$ (2)

Oral Cancer Potency Factor: 0.0075 (mg/kg/day)⁻¹ (1)

Inhalation Cancer Unit Risk: 0.00000047 ($\mu\text{g}/\text{m}^3$)⁻¹ (1)

In rats administered single oral doses of nonradioactive methylene chloride in water (Angelo, et al., 1986), the amount of methylene chloride remaining in the lower gastrointestinal tract accounted for less than 2% of the administered dose. In a second study (McKenna and Zempel, 1981), a single oral dose of ¹⁴C-DCM administered to rats was eliminated 100% in the breath as unchanged methylene chloride and as metabolites within 48 hours. Both studies suggest close to a 100% oral absorption efficiency.

McKenna, M.J., Zempel, J.A. (1981) *The Dose-Dependent Metabolism of ¹⁴C Methylene Chloride Following Oral Administration to Rat.* Food Cosmet. Toxicol. 19:73-78.

Angelo, M.J., Pritchard, A.B., Hawkins, D.R., Waller, A.R. and Roberts, A. (1986) *The Pharmacokinetics of Dichloromethane. II. Disposition in Fischer 344 Rats Following Intravenous and Oral Administration.* Food Chem. Toxicol. 24:975-980.

No studies were located quantifying the dermal absorption of methylene chloride. Assume it to be similar to the conservative estimate of 10% derived for benzene in a non-occluded dosing protocol.

The oral and dermal cancer potency value for methylene chloride is based on an oral drinking water study in mice. This toxicity value is not based on absorbed dose.

METHYLENE CHLORIDE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal chronic reference dose for methylene chloride is based on an oral drinking water study in rats. In this study, an applied dose was used.

METHYLENE CHLORIDE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for methylene chloride is based on an oral drinking water study in rats. In this study, an applied dose was used.

METHYLENE CHLORIDE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

METHYL ETHYL KETONE

CAS #: 78933

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.5 mg/kg/day (2)

Chronic Oral Reference Dose: 0.05 mg/kg/day (2)

Subchronic Inhalation Reference Concentration: 3000 $\mu\text{g}/\text{m}^3$ (2)

Chronic Inhalation Reference Concentration: 1000 $\mu\text{g}/\text{m}^3$ (1)

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: NC

No information was located to quantitatively determine the oral or dermal absorption efficiency of methyl ethyl ketone. Assume a 100% absorption efficiency by the oral route and a 10% dermal absorption efficiency (non-occluded, 24 hour).

The oral and dermal chronic reference dose for methyl ethyl ketone is based on an inhalation study conducted in rats. An absorption efficiency of 50% was used to calculate an absorbed dose. The RAFs to be used for all exposure pathways are the absorption efficiencies of methyl ethyl ketone by the route in question.

METHYL ETHYL KETONE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.1	1	1

The oral and dermal subchronic reference dose for methyl ethyl ketone is based on an inhalation study conducted in rats. An absorption efficiency of 50% was used to calculate an absorbed dose. The RAFs to be used for all exposure pathways are the absorption efficiencies of methyl ethyl ketone by the route in question.

METHYL ETHYL KETONE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.1	1	1

METHYL TERTIARY BUTYL ETHER

CAS #: 1634044

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.052 mg/kg/day (2)

Chronic Oral Reference Dose: 0.0052 mg/kg/day (2)

Subchronic Inhalation Reference Concentration: 500 $\mu\text{g}/\text{m}^3$ (1c)

Chronic Inhalation Reference Concentration: 500 $\mu\text{g}/\text{m}^3$ (1)

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: NC

No information was located to quantitatively determine the oral or dermal absorption efficiency of methyl tert butyl ether. Assume a 100% absorption efficiency by the oral route and a 10% dermal absorption efficiency (non-occluded, 24 hour).

The oral and dermal chronic reference dose for methyl tert butyl ether is based on an inhalation study conducted in rats. An absorption efficiency of 50% was used to calculate an absorbed dose. The RAFs to be used for all exposure pathways are the absorption efficiencies of methyl tert butyl ether by the route in question.

METHYL TERT BUTYL ETHER RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.1	1	1

The oral and dermal subchronic reference dose for methyl tert butyl ether is based on an inhalation study conducted in rats. An absorption efficiency of 50% was used to calculate an absorbed dose. The RAFs to be used for all exposure pathways are the absorption efficiencies of methyl tert butyl ether by the route in question.

METHYL TERT BUTYL ETHER RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.1	1	1

**NAPHTHALENE and
2-METHYLNAPHTHALENE**

CAS #: 91203

CAS #: 91576

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.04 mg/kg/day (2)

Chronic Oral Reference Dose: 0.04 mg/kg/day (2)

Subchronic Inhalation Reference Concentration: 71 $\mu\text{g}/\text{m}^3$ (3a)

Chronic Inhalation Reference Concentration: 71 $\mu\text{g}/\text{m}^3$ (3b)

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: NC

Oral absorption, based on fecal recovery of metabolites, has been demonstrated to be essentially 100% in the rat (Chang, 1943).

Chang, L H. (1943) *The Fecal Excretion of Polycyclic Hydrocarbons Following Their Administration to the Rat*. J. Biol. Chem. 151:93-102.

No information exists quantifying the dermal absorption efficiency of naphthalene. However, toxicity has been documented following exposure by this suggesting absorption has occurred. Assume 10% to represent the dermal absorption efficiency (same as non-occlude, 24 hour benzene value).

The oral and dermal chronic reference dose for naphthalene and 2-methylnaphthalene is based on an oral gavage study conducted in rats. In this study, an applied dose was used.

NAPHTHALENE & 2-METHYLNAPHTHALENE RAFs
Evaluation of Chronic Exposures

SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for naphthalene and 2-methylnaphthalene is based on an oral gavage study conducted in the rats. In this study, an applied dose was used.

NAPHTHALENE & 2-METHYLNAPHTHALENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.02 mg/kg/day (2)

Chronic Oral Reference Dose: 0.02 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: Not Volatile

Human and animal studies indicate that the oral absorption efficiency of nickel from food or water ranges from 1% - 10% (Christensen and Lagesson, 1981; Schroeder et al., 1974; Tedeschi and Sunderman, 1956; Ambrose et al., 1976; Nielsen et al., 1986; Ho and Furst, 1973). The upper-bound of 10% is selected as a protective estimate of the oral absorption efficiency of nickel.

Christensen, O.B. and Lagesson, V. (1981) *Nickel Concentrations of Blood and Urine After Oral Administration*. *Ann. Clin. Lab. Sci.* 11:119-125.

Schroeder, H.A., Mitchener, M. and Nason, A.P. (1974) *Life-Term Effects of Nickel in Rats: Survival, Tumors, Interactions with Trace Elements and Tissue Levels*. *J. Nutr.* 104:239-243.

Tedeschi, R.E. and Sunderman, F.W. (1957) *Nickel Poisoning V. The Metabolism of Nickel Under Normal Conditions and After Exposure to Nickel Carbonyl*. *Arch. Ind. Health* 16:486-488.

Ambrose, A.M., Larson, P.S., Borzelleca, J.R. and Hennigar, G.R. (1976) *Long Term Toxicologic Assessment of Nickel in Rats and Dogs*. *J. Food. Sci. Technol.* 13:181-187.

Nielsen, G.D., Andersen, O., Jensen, M. and Grandjean, P. (1986) *Gastrointestinal Nickel Absorption. A New Experimental Model Using the Gamma-Emitting Isotope ⁵⁷Ni*. In: *The Sixth UOEH Int. Symp., 3rd COMTOX on Bio- and Toxicokinetics of Metals*, Kitakyushu City, Japan, Int. Conf. Clin. Chem., Chem. Toxicol., July 27-31.

Ho., W. and Furst, A. (1973) *Nickel Excretion by Rats Following a Single Treatment*. *Proc. West. Pharmacol. Soc.* 16:245-248.

Aqueous solutions of various forms of nickel can penetrate occluded human skin with absorption efficiencies ranging from 55% - 77%, most absorption occurring in the first 24 hours (Norgaard, 1955). It is unclear whether the nickel was absorbed into the deep layers of the skin or into the bloodstream. Studies in guinea pigs (Lloyd, 1980) demonstrated that much of the nickel absorbed remained in the skin, primarily in the highly keratinized areas, while approximately 0.005 - 0.51 % of the applied nickel chloride was recovered from the blood and urine. A more recent study on excised human skin (Fullerton et al., 1986) indicated that 3.5% of an applied dose of nickel chloride

permeated the skin after 144 hours when the skin was occluded. Fullerton also noted that nickelous ions from a chloride solution passed through the skin \approx 50 times faster than nickelous ions from a sulfate solution.

An absorption value of 3.5% is selected as an realistic estimate applicable to human exposure scenarios.

Fullerton, A., Anderson, J.R., and Hoelgaard, A. et al. (1986) *Permeation of nickel salts through human skin in vitro*. *Cont. Derma.* 15:173-177.

Lloyd, G.K. (1980) *Dermal absorption of nickel in relation to the induction of allergic contact dermatitis: Preliminary results*. In: *Nickel Toxicology*, Brown, S.S. and Sunderman, F.W., eds., Academic Press, London U.K.

Norgaard, O. (1955) *Investigation with Radioactive Ni-57 Into the Resorption of Nickel Through the Skin in Normal and in Nickel-Hypersensitive Persons*. *Acta. Derm. Venereol.* 35:111-117.

The oral and dermal chronic reference dose for nickel is based on an oral feeding (dietary) study conducted in rats. In this study, an applied dose was used.

NICKEL RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.1}{0.1} = 1$	$\frac{0.035}{0.1} = 0.35$	$\frac{0.1}{0.1} = 1$	$\frac{0.1}{0.1} = 1$

The oral and dermal subchronic reference dose for nickel is based on an oral feeding (dietary) study conducted in rats. In this study, an applied dose was used.

NICKEL RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.1}{0.1} = 1$	$\frac{0.035}{0.1} = 0.35$	$\frac{0.1}{0.1} = 1$	$\frac{0.1}{0.1} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.04 mg/kg/day (2b)

Chronic Oral Reference Dose: 0.04 mg/kg/day (2f)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: NC

No specific quantitative information found on the absorption via the oral or dermal route. Assume same as B[a]P.

The oral and dermal chronic reference dose for phenanthrene is based on a naphthalene oral gavage study in rats. In this study, an applied dose was used.

PHENANTHRENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

The oral and dermal subchronic reference dose for phenanthrene is based on a naphthalene oral gavage study conducted in rats. In this study, an applied dose was used.

PHENANTHRENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{1} = 0.91$	$\frac{0.18}{1} = 0.18$	$\frac{0.91}{1} = 0.91$	$\frac{0.91}{1} = 0.91$

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PHENOL

CAS #: 108952

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.6 mg/kg/day (2)

Chronic Oral Reference Dose: 0.6 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: Not Volatile

Phenol is absorbed readily and efficiently from the GI tract. In humans, Capel et al. (1972) reported that up to 98% of an oral dose was recovered as urinary metabolites within 24 hours, suggesting 100% absorption. The oral absorption in other species appears to be similar to humans.

Capel, I.D., French, M.R. and Millburn, P. (1972) *Fate of [¹⁴]-phenol in various species. Xenobiotica 2:25-34.*

Phenol is absorbed quite readily from the skin. In one study (Baranowska-Dutkiewicz, 1981), the dermal absorption efficiency of aqueous phenol through human skin was shown to be approximately 13% of the applied dose in 30 minutes (26% in one hour). The value of 26% is assumed to be a protective estimate since volatilization of any remaining phenol is expected to be complete after 1 hour.

Baranowska-Dutkiewicz, B. (1981) *Skin absorption of phenol from aqueous solutions in men. Int. Arch. Environ. Health 49:99-104.*

The oral and dermal chronic reference dose for phenol is based on an oral gavage study (via water) in rats. In this study, an applied dose was used.

PHENOL RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.26}{1} = 0.26$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for phenol is based on an oral gavage study (via water) in rats. In this study, an applied dose was used.

PHENOL RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.26}{1} = 0.26$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose: 0.000005 mg/kg/day (4)****Chronic Oral Reference Dose: 0.000005 mg/kg/day (4)****Subchronic Inhalation Reference Concentration: Not Volatile****Chronic Inhalation Reference Concentration: Not Volatile****Oral Cancer Potency Factor: 7.7 (mg/kg/day)⁻¹ (1)****Inhalation Cancer Unit Risk: Not Volatile**

Oral (gavage) studies in rats and rhesus monkeys demonstrate a range in absorption efficiencies of PCBs to be 90%-99% (Albro and Fishbein, 1972; Allen et al., 1974). When administered to ferrets in food, 85% of an applied dose was seen to be absorbed (Bleavins et al., 1984). The oral absorption efficiency of ¹⁴C-labeled PCB contaminated soil and pure ¹⁴C-labeled PCBs was assessed in Sprague-Dawley rats (Fries et al., 1989). The absorption efficiencies were reported as follows:

	Soil/diet	Soil/gavage	Non-soil/diet	Non-soil/gavage
TriPCBs	82%	78%		
TetraPCBs	80%	89%	91%	95%
PentaPCBs	<u>67%</u>	<u>78%</u>	<u>86%</u>	<u>81%</u>
Average	76%	82%	89%	88%

These results suggest that the presence of soil does inhibit the oral absorption of PCBs.

Fries, G.F., Marrow, G.S. and Somich, C.J. (1989) *Oral Bioavailability of Aged Polychlorinated Biphenyl Residues Contained in Soil*. Bull. Environ. Contam. Toxicol. 43:683-690.

Albro, P.W. and Fishbein, L. (1972) *Intestinal Absorption of Polychlorinated Biphenyls in Rats*. Bull. Environ. Contam. Toxicol. 8:26-35.

Allen, J.R., Norback, D.H., Hsu, I.C. (1974) *Tissue Modifications in Monkeys as Related to Absorption, Distribution and Excretion of Polychlorinated Biphenyls*. Arch. Environ. Contam. Toxicol. 2:86-95.

Bleavins, M.R., Breslin, W.J., Aulerich, R.J. and Ringer, R.K. (1984) *Placental and Mammary Transfer of a Polychlorinated Biphenyl Mixture (Aroclor 1254) in the European Ferret*. Environ. Toxicol. Chem. 3:637-44.

The dermal absorption efficiency (24 hour) of ¹⁴C-PCBs in guinea pigs ranged from 33% - 56% of the applied dose, dependent on the concentration applied. The range in Rhesus monkeys was 15% - 34% of the applied dose. These ranges were based on excretion of radioactivity in urine and feces. Assume the upper-bound estimate of 56% is representative and protective for human exposure to pure compound. Roy et al. (1989) examined the dermal absorption of tetraPCBs in low organic carbon content soil in rats. After 96 hours, 50% of the applied dose had been absorbed. Assuming linearity, this suggests 12.5% absorption of soil-associated PCBs in 24 hours.

A recent U.S. EPA study (US EPA, 1992) recommended absorption efficiencies for PCBs in soil for human skin between 0.6% (high carbon soils) and 6% (low carbon soils).

Roy, T.A., Yang, J.J., Krueger, A.J., Driver, J.H. and Konz, J.J. (1989) Dermal Absorption of Dioxins and PCBs from Soil. Draft report prepared by Versar, Inc. for U.S. EPA, Office of Toxic Substances, Exposure Evaluation Division, Exposure Assessment Branch. EPA Contract No. 68-02-4254.

US EPA (1992), Dermal Absorption Assessment: Principles and Applications. EPA/600/8-91/011B. Office of Research and Development, Washington D.C.

Wester, R.C., Bucks, D.A.W., Maibach, H.I. and Anderson, J. (1983) *Polychlorinated Biphenyls (PCBs): Dermal Absorption, Systemic Elimination and Dermal Wash Efficiency*. *J. Toxicol. Environ. Health* 12:511-519.

The oral and dermal cancer potency value for PCBs is based on an oral feeding (dietary) study in rats. This toxicity value is not based on absorbed dose.

PCBs RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.76}{0.89} = 0.85$	$\frac{0.06}{0.89} = 0.067$	$\frac{0.89}{0.89} = 1$	$\frac{0.89}{0.89} = 1$

The oral and dermal chronic reference dose for PCBs is based on an oral feeding (dietary) study in primates. In this study, an applied dose was used.

PCBs RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.76}{0.89} = 0.85$	$\frac{0.06}{0.89} = 0.067$	$\frac{0.89}{0.89} = 1$	$\frac{0.89}{0.89} = 1$

The oral and dermal subchronic reference dose for PCBs is based on an oral feeding (dietary) study in primates. In this study, an applied dose was used.

PCBs RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.76}{0.89} = 0.85$	$\frac{0.06}{0.89} = 0.067$	$\frac{0.89}{0.89} = 1$	$\frac{0.89}{0.89} = 1$

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PYRENE

CAS #: 129000

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.3 mg/kg/day (2)

Chronic Oral Reference Dose: 0.03 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: Not Volatile

No specific quantitative information found on the absorption via the oral or dermal route.
Assume same as B[a]P.

The oral and dermal chronic reference dose for pyrene is based on an oral gavage study conducted in mice. In this study, an applied dose was used.

PYRENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

The oral and dermal subchronic reference dose for pyrene is based on an oral gavage study conducted in mice. In this study, an applied dose was used.

PYRENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.91}{0.91} = 1$	$\frac{0.18}{0.91} = 0.2$	$\frac{0.91}{0.91} = 1$	$\frac{0.91}{0.91} = 1$

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TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose: 0.005 mg/kg/day (1e)****Chronic Oral Reference Dose: 0.005 mg/kg/day (1)****Subchronic Inhalation Reference Concentration: Not Volatile****Chronic Inhalation Reference Concentration: Not Volatile****Oral Cancer Potency Factor: NC****Inhalation Cancer Unit Risk: Not Volatile**

The oral absorption efficiency of silver compounds varies between species. Estimates range from 1% in rats and mice, 10% in dogs (Furchner et al., 1968) and 21% in humans (MacIntyre et al., 1978). Furchner considered their calculated equilibrium factor of 4.4% to be a conservative estimate for the amount of silver retained by a 70 kg human. The differences are believed to be due to differences in gastrointestinal transit times between species.

Furchner, J.E., Richmond, C.R. and Drake, G.A. (1968) *Comparative Metabolism of Radionuclides in Mammals - IV. Retention of Silver-110m in the Mouse, Rat, Monkey and Dog.* *Health Phys.* 15:505-514.

MacIntyre, D., Mclay, A.L.C. and East, B.W. (1978) *Silver Poisoning Associated with an Antismoking Lozenge.* *Br. Med. J.* 2:1749-1750.

Less than 1% of dermally-applied silver compounds are absorbed through the intact skin of humans (Snyder et al., 1985). The amount dermally absorbed by guinea pigs was estimated to be approximately 1% of the applied dose (Wahlberg, 1965).

Snyder, W.S., et al. (1975) Report of the Task Group on Reference Man. Oxford, England: Pergamon Press, pp. 407-708.

Wahlberg, J.E. (1965) *Percutaneous Toxicity of Metal Compounds. A Comparative Investigation in Guinea Pigs.* *Arch. Environ. Health* 11:201-204.

The oral and dermal chronic reference dose for silver is based on a human intravenous study converted to an applied oral dose assuming 4% oral retention.

SILVER RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.04}{0.04} = 1$	$\frac{0.01}{0.04} = 0.25$	$\frac{0.04}{0.04} = 1$	$\frac{0.04}{0.04} = 1$

The oral and dermal subchronic reference dose for silver is based on a human intravenous study converted to an applied oral dose assuming 4% retention.

SILVER RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.04}{0.04} = 1$	$\frac{0.01}{0.04} = 0.25$	$\frac{0.04}{0.04} = 1$	$\frac{0.04}{0.04} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.1 mg/kg/day (2)

Chronic Oral Reference Dose: 0.01 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: 4600 $\mu\text{g}/\text{m}^3$ (3a)Chronic Inhalation Reference Concentration: 4600 $\mu\text{g}/\text{m}^3$ (3)Oral Cancer Potency Factor: 0.052 (mg/kg/day)⁻¹ (2h)Inhalation Cancer Unit Risk: 0.00000058 ($\mu\text{g}/\text{m}^3$)⁻¹ (2h)

Results from several animal studies (Pegg et al., 1979; Schumann et al., 1980; Frantz and Wantanabe, 1983) indicate that tetrachloroethylene is rapidly and virtually completely absorbed following oral administration.

Frantz, S.W. and Wantanabe, P.G. (1983) *Tetrachloroethylene: Balance and Tissue Distribution in Male Sprague-Dawley Rats by Drinking Water Administration*. *Toxicol. Appl. Pharmacol.* 69:66-72.

Pegg, D.G., Zemple, J.A., Braun, W.H. and Watanabe, P.G. (1979) *Disposition of (¹⁴C)Tetrachloroethylene Following Oral and Inhalation Exposure in Rats*. *Toxicol. Appl. Pharmacol.* 51:465-474.

Schumann, A.M., Quast, J.F., and Watanabe, P.G. (1980) *The Pharmacokinetics and Macromolecular Interactions of Perchloroethylene in Mice and Rats as Related to Oncogenicity*. *Toxicol. Appl. Pharmacol.* 55:207-219.

Dermal absorption of tetrachloroethylene appears to be poor (0.24 mg/cm²/hr) (Tsuruta, 1975). Therefore, the absorption efficiency by the dermal route in a non-occluded exposure probably does not exceed 10% (see benzene).

Tsuruta, H. (1975) *Percutaneous absorption of organic solvents. I. Comparative study of +6 percutaneous absorption of chlorinated solvents in mice*. *Ind. Health* 13:227-236.

The oral and dermal cancer potency value for tetrachloroethylene is based on a gavage study in mice. This toxicity value is not based on absorbed dose.

TETRACHLOROETHYLENE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal chronic reference dose for tetrachloroethylene is based on an oral gavage (via corn oil) in mice. In this study, an applied dose was used.

TETRACHLOROETHYLENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for tetrachloroethylene is based on an oral gavage (via corn oil) study in mice. In this study, an applied dose was used.

TETRACHLOROETHYLENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.0007 mg/kg/day (2)

Chronic Oral Reference Dose: 0.00007 mg/kg/day (2)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: Not Volatile

Limited human data suggest that most of an oral dose of thallium (applied as thallium nitrate) is absorbed from the gastrointestinal tract (Barclay et al., 1953). Animal studies suggest that thallium is completely absorbed when ingested. A single trace dose of thallium²⁰⁴ (as thallium nitrate) was administered orally to rats (Lie et al., 1960). The body burden of thallium²⁰⁴, as percent dose, decreased with a single exponential function which extrapolated to 100% at zero time. It was concluded that thallium is completely absorbed from the gastrointestinal tract. A 100% oral absorption efficiency is therefore assumed for thallium compounds.

Barclay, R.K., Pencock, W.C., Kanofsy, D.A. (1953) *Distribution and Excretion of Radioactive Thallium in the Chick Embryo, Rat and Man*. J. Pharmacol. Exp. Ther. 107:178-187.

Lie, R., Thomas, R. and Scott, J. (1960) *The Distribution and Excretion of Thallium²⁰⁴ in the Rat, with Suggested MPC's and a Bio-Assay Procedure*. Health Phys. 2:334-340.

No quantitative studies were located regarding the dermal absorption of thallium in humans or animals. Assume a dermal absorption efficiency of 1% as a conservative upper-bound estimate (see chromium).

The oral and dermal chronic reference dose for thallium is based on an oral study conducted in rats. In this study, an applied dose was used.

THALLIUM RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.01}{1} = 0.01$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for thallium is based on an oral study conducted in rats. In this study, an applied dose was used.

THALLIUM RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.01}{1} = 0.01$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 2 mg/kg/day (2)

Chronic Oral Reference Dose: 0.2 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: 2000 $\mu\text{g}/\text{m}^3$ (2)

Chronic Inhalation Reference Concentration: 400 $\mu\text{g}/\text{m}^3$ (1)

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: NC

Rabbit studies indicate that essentially 100% of an oral dose of toluene is either excreted as metabolites or exhaled unchanged, implying 100% absorption efficiency by the oral route (Smith et al., 1954; El Masry et al., 1956). Oral absorption efficiency of soil-adsorbed toluene was not changed from that of the pure compound even though absorption was delayed in time by the presence of sandy soil (Turkall et al., in press).

El Masry, A.M., Smith, J.N. and Williams, R.T. (1956) *Studies in Detoxication* 69. *The Metabolism of Alkylbenzenes: n-Propylbenzene and n-Butylbenzene with Further Observations on Ethylbenzene*. *Biochem. J.* 64:50-56.

Smith, J.N., Smithies, R.H. and Williams, R.T. (1954) *Studies in Detoxication* 55. *The Metabolism of Alkylbenzenes*. *Biochem. J.* 56:317-325.

Turkall, R.M., Skowronski, G.A. and Abdel-Rahmen, M.S. (in press) *Differences in Kinetics of Pure and Soil-Adsorbed Toluene in Orally Exposed Male Rats*. *Arch. Environ. Contam. Toxicol.*

The dermal absorption of toluene has been measured to be approximately 2% of the applied dose in 4 hours, or 12% in 24 hours (Susten et al., 1990). This study allowed for volatilization of toluene, rapidly decreasing the actual applied dose. In a second study (Skowronski, et al., 1989), volatilization loss was minimized to less than 10% of the applied dose by occlusion. The dermal absorption efficiency was estimated to be approximately 90% with volatilization loss accounting for the remainder of the dose (essentially 100% dermal absorption). The estimate was based on recovery of radioactivity in urine, feces and expired air. The dermal absorption of toluene was unaffected by its adsorption to clay or sandy soils. The 24 hour non-occluded value (12%) is assumed to be the most appropriate and protective for human exposure.

Susten, A.S., Niemeier, R.W. and Simon, S.D. (1990) *In Vivo Percutaneous Absorption Studies of Volatile Organic Solvents in Hairless Mice II. Toluene, Ethylbenzene and Aniline*. *J. Appl. Toxicol.* 10:217-225.

Skowronski, G.A., Turkall, R.M. and Abdel-Rahman, M.S. (1989) *Effects of Soil on Percutaneous Absorption of Toluene in Male Rats*. *J. Toxicol. Environ. Health* 26:373-384.

The oral and dermal chronic reference dose for toluene is based on an oral gavage (via corn oil) study conducted in rats. In this study, an applied dose was used.

TOLUENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.12}{1} = 0.12$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for toluene is based on an oral gavage (via corn oil) study conducted in rats. In this study, an applied dose was used.

TOLUENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.12}{1} = 0.12$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:**Subchronic Oral Reference Dose: 0.9 mg/kg/day (2)****Chronic Oral Reference Dose: 0.09 mg/kg/day (2)****Subchronic Inhalation Reference Concentration: 10000 $\mu\text{g}/\text{m}^3$ (2)****Chronic Inhalation Reference Concentration: 1000 $\mu\text{g}/\text{m}^3$ (2)****Oral Cancer Potency Factor: NC****Inhalation Cancer Unit Risk: NC**

No studies were located containing information to quantitate the oral absorption efficiency of 1,1,1-trichloroethane. However, it can be assumed to be rapidly and completely absorbed in a manner similar to other chlorinated volatiles.

No studies were located containing information to quantitate the dermal absorption efficiency of 1,1,1-trichloroethane. Assume a 10% absorption efficiency (non-occluded, 24 hour), comparable to other volatile compounds.

The oral and dermal chronic reference dose for 1,1,1-trichloroethane is based on an inhalation study conducted in guinea pigs. An absorption efficiency of 30% was used to calculate an absorbed dose. The RAFs to be used for all exposure pathways are the absorption efficiencies of 1,1,1-trichloroethane by the route in question.

1,1,1-TRICHLOROETHANE RAFs
Evaluation of Chronic Exposures

SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.1	1	1

The oral and dermal subchronic reference dose for 1,1,1-trichloroethane is based on an inhalation study conducted in guinea pigs. An absorption efficiency of 30% was used to calculate an absorbed dose. The RAFs to be used for all exposure pathways are the absorption efficiencies of 1,1,1-trichloroethane by the route in question.

1,1,1-TRICHLOROETHANE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.1	1	1

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.02 mg/kg/day (4)

Chronic Oral Reference Dose: 0.002 mg/kg/day (4)

Subchronic Inhalation Reference Concentration: 180 $\mu\text{g}/\text{m}^3$ (3a)Chronic Inhalation Reference Concentration: 180 $\mu\text{g}/\text{m}^3$ (3)Oral Cancer Potency Factor: 0.011 (mg/kg/day)⁻¹ (2h)Inhalation Cancer Unit Risk: 0.0000017 ($\mu\text{g}/\text{m}^3$)⁻¹ (2h)

Oral absorption studies in experimental animals indicate that trichloroethylene is extensively absorbed by the oral route. Absorption efficiency was measured as 91% - 98% of an applied oral dose (Prout et al., 1985; Dekant et al., 1984) determined as radioactivity in expired air and urine. Radioactivity in the carcass was not determined. Absorption, therefore, is assumed to be complete.

Dekant, W., Metzler, M. and Henschler, D. (1984) *Novel Metabolites of Trichloroethylene Through Dechlorination Reactions in Rats, Mice and Humans*. *Biochem. Pharmacol.* 33:2021-2027.

Prout, M.S., Provan, W.M. and Green, T. (1985) *Species Differences in Response to Trichloroethylene*. *Toxicol. Appl. Pharmacol.* 79:389-400.

No studies were located regarding the dermal absorption efficiency of trichloroethylene. Assume 10% dermal absorption (non-occluded, 24 hour) based on physical and chemical properties similar to the other volatile compounds.

The oral and dermal cancer potency value for trichloroethylene is based on a gavage study in mice. This toxicity value is not based on absorbed dose.

TRICHLOROETHYLENE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.1}{1} = 0.1$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal chronic reference dose for trichloroethylene is based on an inhalation study in rats. An absorption factor of 30% was used to calculate an absorbed dose. The RAFs to be used for all exposure pathways are the absorption efficiencies of trichloroethylene by the route in question.

TRICHLOROETHYLENE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.1	1	1

The oral and dermal subchronic reference dose for trichloroethylene is based on an inhalation study in rats. An absorption factor of 30% was used to calculate an absorbed dose. The RAFs to be used for all exposure pathways are the absorption efficiencies of trichloroethylene by the route in question.

TRICHLOROETHYLENE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
1	0.1	1	1

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.001 mg/kg/day (4)

Chronic Oral Reference Dose: 0.001 mg/kg/day (4)

Subchronic Inhalation Reference Concentration: 17 $\mu\text{g}/\text{m}^3$ (3a)

Chronic Inhalation Reference Concentration: 17 $\mu\text{g}/\text{m}^3$ (3)

Oral Cancer Potency Factor: 1.9 (mg/kg/day)⁻¹ (2)

Inhalation Cancer Unit Risk: 0.000084 ($\mu\text{g}/\text{m}^3$)⁻¹ (2)

In young human volunteers administered vinyl chloride monomer for 6 hours, an average retention of 42% was estimated. It was not reported whether steady state had been achieved. Maximum retention was achieved at 15 minutes and retention declined after 30 minutes after which it increased to a relatively constant value. The percentage retained seemed to be independent of the concentration inhaled. A range of reported inhalation absorption efficiencies is 40% - 98%, 64% being suggested as representative and protective (Owen, 1990)

Owen, B.A. (1990) *Literature-Derived Absorption Coefficients for 39 Chemicals Via Oral and Inhalation Routes of Exposure*. Regul. Toxicol. Pharmacol. 11:237-252.

Krajewski, J., Dobecki, M. and Gromiec, J. (1980) *Retention of Vinyl Chloride in the Human Lung*. Br. J. Ind. Med. 37:373-374.

Rats were administered single gavage doses of ¹⁴C-vinyl chloride in corn oil and radioactivity levels excreted in expired air, urine and feces, as well as the amount remaining in the carcass, were measured at 72 hours. 0.47-2.39% of the administered dose was recovered in the feces indicating that absorption was nearly complete. Total recovery ranged from 82.3-91.3% suggesting a substantial loss of radioactivity. An oral absorption efficiency of 98% is assumed to be protective for human exposure.

Watanabe, P.G., McGowan, G.R. and Gehring, P.J. (1976) *Fate of [¹⁴C] Vinyl Chloride After Single Oral Administration*. Toxicol. Appl. Pharmacol. 36:339-352.

Two rhesus monkeys exposed from the neck down to ¹⁴C-vinyl chloride vapor were found to have dermal absorptions of 0.031% and 0.023%, respectively. The dermal absorption of neat vinyl chloride or soil contaminated with vinyl chloride would be expected to be greater due to increased time of dermal contact. Therefore, the dermal absorption efficiency is assumed to be similar to the 10% estimate derived for other volatile compounds (non-occluded, 24 hour).

The oral and dermal cancer potency value for vinyl chloride is based on an inhalation study in rats. This toxicity value is not based on absorbed dose.

VINYL CHLORIDE RAFs Evaluation of Carcinogenicity			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.98}{0.64} = 1.53$	$\frac{0.1}{0.64} = 0.16$	$\frac{0.98}{0.64} = 1.53$	$\frac{0.98}{0.64} = 1.53$

The oral and dermal chronic reference dose for vinyl chloride is based on an oral feeding (dietary) study in rats. In this study, an applied dose was used.

VINYL CHLORIDE RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.98}{0.98} = 1$	$\frac{0.1}{0.98} = 0.1$	$\frac{0.98}{0.98} = 1$	$\frac{0.98}{0.98} = 1$

The oral and dermal subchronic reference dose for vinyl chloride is based on an oral feeding (dietary) study in rats. In this study, an applied dose was used.

VINYL CHLORIDE RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.98}{0.98} = 1$	$\frac{0.1}{0.98} = 0.1$	$\frac{0.98}{0.98} = 1$	$\frac{0.98}{0.98} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 4 mg/kg/day (2)

Chronic Oral Reference Dose: 2 mg/kg/day (1)

Subchronic Inhalation Reference Concentration: 300 $\mu\text{g}/\text{m}^3$ (2)

Chronic Inhalation Reference Concentration: 300 $\mu\text{g}/\text{m}^3$ (2)

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: NC

The oral absorption efficiency of 100% is estimated from limited excretion data specifying that more than 98% of an oral dose of p-xylene was absorbed and excreted as metabolites in urine and expired air of the rabbit.

Bray, H.G., Humphric, B.G. and Thorpe, W.V. (1949) *Metabolism of Derivatives of Toluene 3. o-,m- and p-Xylenes*. *Biochem. J.* 45:241-244.

The dermal absorption efficiency of m-xylene, adsorbed to either sand or clay, has been demonstrated to be essentially 100% of an occluded dose when applied to the shaved skin of male rats (Skowronski et al., 1990). Absorption was rapid with 50% of the dose absorbed in less than 1 hour. Soil adsorption slightly delayed the dermal absorption of m-xylene relative to pure parent compound. The dermal absorption of soil adsorbed mixed xylene isomers is assumed to behave as m-xylene. No information exists on non-occluded dermal uptake, however, it would be assumed to be similar to that of its structural analog, toluene (12% in 24 hours).

Skowronski, G.A., Turkall, R.M., Kadry, A.R.M. and Abdel-Rahmen, M.S. (1990) *Effects of soil on the dermal bioavailability of m-xylene in male rats*.

The oral and dermal chronic reference dose for xylenes is based on an oral gavage study conducted in rats. In this study, an applied dose was used.

XYLENES RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.12}{1} = 0.12$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

The oral and dermal subchronic reference dose for xylenes is based on an oral gavage study conducted in rats. In this study, an applied dose was used.

XYLENES RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{1}{1} = 1$	$\frac{0.12}{1} = 0.12$	$\frac{1}{1} = 1$	$\frac{1}{1} = 1$

TOXICITY INFORMATION FROM THE RESIDENTIAL SHORTFORM:

Subchronic Oral Reference Dose: 0.2 mg/kg/day (2)

Chronic Oral Reference Dose: 0.2 mg/kg/day (2)

Subchronic Inhalation Reference Concentration: Not Volatile

Chronic Inhalation Reference Concentration: Not Volatile

Oral Cancer Potency Factor: NC

Inhalation Cancer Unit Risk: Not Volatile

The absorption of zinc in humans from the diet has been determined to range from 22% - 46% (Sandstrom et al., 1987) with the upper limit of the range suggested as an appropriate estimate. Zinc is more efficiently absorbed from drinking water with absorption estimates ranging up to 58% (Dinsmore et al., 1985; Farah et al., 1984; Valberg et al., 1985).

Dinsmore, W., Callender, M.E., McMaster, D., Todd, S.J. and Love, A.H.G. (1985) *Zinc Absorption in Alcoholics Using Zinc-65*. *Digest*. 32:238-242.

Farah, D.A., Hall, M.J., Mills, P.R. and Russell, R.I. (1984) *Effect of Wheat Bran on Zinc Absorption*. *Human Nutr. Clin. Nutr.* 38C:433-441.

Sandstrom, B., Davison, L., Kivisto, B., Hasselbland, C. and Cederbland, A. (1987) *The Effect of Vegetables and Beet Fibre on the Absorption of Zinc in Humans from Composite Meals*. *Brit. J. Nutr.* 58:49-57.

Valberg, L.S., Flanagan, P.R., Ghent, C.N. and Chamberlai, M.J. (1985) *Zinc Absorption and Leukocyte Zinc in Alcoholic and Nonalcoholic Cirrhosis*. *Digest. Dis. Sci.* 30:329-333.

No studies were located quantitatively describing the dermal absorption of zinc compounds. Assume a dermal absorption efficiency of 1% as a conservative upper-bound estimate (see chromium).

The oral and dermal chronic reference dose for zinc is based on an oral human dietary study. In this study, an applied dose was used.

ZINC RAFs Evaluation of Chronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.46}{0.46} = 1$	$\frac{0.01}{0.46} = 0.02$	$\frac{0.58}{0.46} = 1.3$	$\frac{0.46}{0.46} = 1$

The oral and dermal subchronic reference dose for zinc is based on an oral human dietary study. In this study, an applied dose was used.

ZINC RAFs Evaluation of Subchronic Exposures			
SOIL INGESTION	SOIL DERMAL	WATER INGESTION	VEGETABLE INGESTION
$\frac{0.46}{0.46} = 1$	$\frac{0.01}{0.46} = 0.02$	$\frac{0.58}{0.46} = 1.3$	$\frac{0.46}{0.46} = 1$

APPENDIX D

MA DEP DERIVED

TOXICITY VALUES

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BENZENE

SUBCHRONIC INHALATION REFERENCE CONCENTRATION

The subchronic inhalation Reference Concentration (RfC) equivalent value was derived from information presented in the Massachusetts DEP's Methodology to Derive Indoor Air Guidance Levels (MA DEP, 1991). The subchronic RfC is based on a 4 week study (Rosenthal, 1987) which examined the effect of inhaled benzene (6 hours/day, 5 days/week) on circulating lymphocytes. The ability of exposed mice to mount a cell-mediated immune response associated with tumor surveillance was monitored and noted to be delayed, suggesting compromised function. A Lowest Observed Adverse Effects Level (LOAEL) of 10 ppm (32.2 mg/m³) was identified by this study as a level of benzene which still resulted in significant impairment of the lymphocyte response. Based on this LOAEL and the application of standard uncertainty factors, a subchronic RfC equivalent may be calculated.

$$UF_1 = 10 = \text{LOAEL} \rightarrow \text{NOAEL}$$

$$UF_2 = 10 = \text{animal} \rightarrow \text{human extrapolation}$$

$$UF_3 = 10 = \text{sensitive subpopulations}$$

$$RfC_{\text{subchronic}} = 32.2 \text{ mg/m}^3 * 10^3 \mu\text{g/mg} * (1/10) * (1/10) * (1/10)$$

$$RfC_{\text{subchronic}} = 32 \mu\text{g/m}^3$$

SUBCHRONIC ORAL REFERENCE DOSE

The subchronic oral Reference Dose equivalent value was derived from information presented in the U.S. EPA's Benzene Health Advisory (U.S. EPA, 1987). The subchronic RfD is based on a study by Deichman (1963) who exposed Sprague-Dawley rats to benzene by inhalation (6 hrs/day, 4 days/week) at a broad range of concentrations and monitored their hematology weekly. By the second week of treatment, there was definite hematological impairment, including severe leukopenia at the 61, 65 and 831 ppm exposure concentrations and moderate leukopenia, especially in females, at the 44 and 47 ppm exposure concentrations. Leukopenia was not observed at 29 or 31 ppm.

Based on this data, and assuming 50% absorption of inhaled benzene (Nomiya, 1974 a,b), a subchronic RfD equivalent may be calculated:

$$NOAEL_{2 \text{ wks exposure}} = 31 \text{ ppm (96 mg/m}^3\text{)}$$

$$AD_{rat} = \frac{96 \text{ mg/m}^3 * 4 \text{ ev/wk} * 6 \text{ hr/ev} * 0.26 \text{ m}^3/\text{d} * 0.5}{0.35 \text{ kg} * 168 \text{ hr/1 wk}}$$

$$AD_{rat} = 5 \text{ mg/kg/day}$$

Where:

AD_{rat} = The calculated Absorbed Dose in the rat study. In units: **mg/kg/day**
 96 mg/m^3 = No Observed Adverse Effects Level (NOAEL)
 4 events/week = dosing regimen from the study
 6 hours/day = dosing regimen from the study
 $0.26 \text{ m}^3/\text{day}$ = rat inhalation rate
 0.5 = absorption efficiency
 0.35 kg = rat body weight
 168 hrs/week = Conversion factor

The AD_{rat} may be converted to an allowable *human* absorbed subchronic reference dose equivalent through the application of standard uncertainty factors:

$UF_1 = 10$ = animal -> human extrapolation

$UF_2 = 10$ = sensitive subpopulations

$$RfD_{subchronic} = 5 \text{ mg/kg/day} * (1/10) * (1/10)$$

$$RfD_{subchronic} = 0.05 \text{ mg/kg/day}$$

CHRONIC ORAL REFERENCE DOSE

The chronic oral Reference Dose (RfD) equivalent was derived from the Deichman study described above. The AD_{rat} calculated above may be converted to an allowable *human* absorbed chronic reference dose equivalent through the application of standard uncertainty factors:

$UF_1 = 10$ = animal -> human extrapolation

$UF_2 = 10$ = sensitive subpopulations

$UF_3 = 10$ = subchronic -> chronic

$$RfD_{chronic} = 5 \text{ mg/kg/day} * (1/10) * (1/10) * (1/10)$$

$$RfD_{chronic} = 0.005 \text{ mg/kg/day}$$

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CYANIDE

SUBCHRONIC INHALATION REFERENCE CONCENTRATION

A subchronic reference concentration (RfC) equivalent value and a chronic allowable threshold concentration (ATC) for cyanide have been developed based on human and animal toxicological information for all forms of inhaled cyanide. The long-term health consequences following inhalation exposure to cyanide are primarily central nervous system effects including deafness, visual deficits and loss of muscular coordination. Other organ systems involved (cardiovascular, thyroid, respiratory) are believed to be secondary responses. No evidence exists to implicate cyanide as possessing carcinogenic properties, however, it is possible that reproductive/developmental effects would result following exposure.

Few studies exist concerning health consequences of long-term cyanide inhalation. Two possible key studies have been identified from a thorough literature search. The study of El Ghawabi et al. (1975) is a human epidemiological study which examined thyroid enlargement in non-smoking workers occupationally exposed to cyanide at levels of 6.4 to 10.4 ppm for 5 to 15 years. It is possible that a chronic human LOAEL of 6.4 ppm could be identified from this study, however, it is likely that the workers were exposed to other volatiles and particulates during the course of their employment. A second key study (Hugod, 1981) involved the examination of myocardial histopathology in rabbits continuously exposed to hydrogen cyanide for 28 days. From this study a subchronic animal NOAEL of 0.5 ppm can be identified. This study is flawed since the investigator did not report a dose-response relationship and by the criticism that other cardiac indices may be more sensitive indicators of cardiac damage (O'Flaherty and Thomas, 1982). However, this study is the only inhalation study available with continuous exposure to cyanide of a subchronic nature.

The subchronic animal NOAEL of 0.5 ppm hydrogen cyanide gas (0.55 mg/m^3 cyanide) from the Hugod study was adjusted according to standard EPA RfC methodology (EPA, 1990) to derive a subchronic RfC for cyanide.

- Animal NOAEL (28-day, continuous, adult) = 0.55 mg/m^3
- Human-Equivalent Concentration ($\times 1.8$) = 0.99 mg/m^3
- Human NOAEL ($\div 10$) = 0.099 mg/m^3
- Adjustment for sensitive individuals ($\div 10$) = 0.0099 mg/m^3
- Low confidence in database ($\div 10$) = 0.00099 mg/m^3

$$\text{SUBCHRONIC RfC} = 1.0 \mu\text{g/m}^3$$

CHRONIC INHALATION REFERENCE CONCENTRATION

According to EPA RfC methodology for gases producing extrarespiratory effects, the air concentration should be adjusted to yield a human-equivalent concentration based on the ratio of the inhalation rate/body weight for the animal and human according to the following equation:

$$\frac{\frac{(\text{Inhalation Rate})_{\text{rabbit}}}{(\text{Body Weight})_{\text{rabbit}}}}{\frac{(\text{Inhalation Rate})_{\text{human}}}{(\text{Body Weight})_{\text{human}}}}$$

The confidence in the database is low since very few inhalation studies are available. Of those studies identified, all are either methodologically flawed or utilize high exposure levels.

The Chemical Health Effects Assessment Methodology (CHEM) (MA DEP, 1990) can be used to derive a threshold effects level (TEL) which is a concentration in air to which the public could be exposed for an average lifetime and experience no adverse threshold health effects. By definition, the TEL incorporates a relative source contribution factor which, when removed, results in an Allowable Threshold Concentration (ATC) (MA DEQE, 1989). The ATC, therefore, is analogous to a chronic RfC.

Occupational limits are used as the basis for a TEL rather than primary toxicity studies. The most appropriate occupational limit (MAOL) for cyanide (inorganic and gaseous forms) of 5 mg/m³ (NIOSH/OSHA) was selected and adjusted to account for continuous exposure and for protection of children and high-risk groups to derive an adjusted MAOL of 0.07 mg/m³.

- MAOL = 5 mg/m³
- Adjustment for continuous exposure (÷ 4.2) = 1.2 mg/m³
- Adjustment for childhood exposure (÷ 1.75) = 0.7 mg/m³
- Adjustment for high-risk groups (÷ 10) = 0.07 mg/m³

$$\text{Adjusted MAOL} = 0.07 \text{ mg/m}^3$$

The adjusted MAOL was further modified to account for reproductive/developmental effects and the relative source contribution which are not considered in setting the occupational exposure limit. Based on available reproductive/developmental studies, cyanide was scored as a category "B" chemical and assigned a threshold effects uncertainty factor (TEUF) of 10.

- TEUF adjustment ($\div 10$) = 0.007 mg/m^3
- Relative source contribution ($\times .2$) = 0.0014 mg/m^3

$$\text{TEL} = 1.4 \text{ } \mu\text{g/m}^3$$

Removing the relative source contribution factor of 0.2 results in the Allowable Threshold Concentration:

$$\text{ATC} = 7 \text{ } \mu\text{g/m}^3$$

or,

$$\text{CHRONIC RfC} = 7 \text{ } \mu\text{g/m}^3$$

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1,2-DICHLOROETHANE

SUBCHRONIC ORAL REFERENCE DOSE

The subchronic oral Reference Dose equivalent value was derived from information presented in the U.S. EPA's 1,2-Dichloroethane Health Advisory (U.S. EPA, 1987). The subchronic RfD is based on a combination of three inhalation studies (Heppel, 1946; Spencer, 1951; Hofmann, 1971) in which various animal species were exposed to 1,2-dichloroethane (1,2-DCA) for up to eight months. In these studies, exposures of rats and guinea pigs to air containing 100 ppm 1,2-dichloroethane for 6 to 7 hours/day, 5 days/week resulted in no mortality and no adverse effects as determined by general appearance, behavior, growth, organ function or blood chemistry. However, similar exposures of rats, guinea pigs, rabbits, and monkeys to air containing 400 to 500 ppm 1,2-dichloroethane resulted in high mortality and varying pathological findings including pulmonary congestion, diffused myocarditis, slight to moderate fatty degeneration of the liver, kidney, adrenal and heart, and increased plasma prothrombin time.

Based on this data, and assuming 30% absorption (U.S. EPA, 1987) of inhaled 1,2-DCA, a subchronic RfD equivalent may be calculated:

$$\text{NOAEL}_{8 \text{ month exposure}} = 100 \text{ ppm (405 mg/m}^3\text{)}$$

$$\text{AD}_{\text{rat}} = \frac{405 \text{ mg/m}^3 * 5 \text{ ev/wk} * 7 \text{ hr/ev} * 0.26 \text{ m}^3/\text{d} * 0.3}{0.35 \text{ kg} * 168 \text{ hr/1 wk}}$$

$$\text{AD}_{\text{rat}} = 19 \text{ mg/kg/day}$$

Where:

AD_{rat}	=	The calculated <u>A</u> bsorbed <u>D</u> ose in the rat study. In units: mg/kg/day
405 mg/m^3	=	No Observed Adverse Effects Level (NOAEL)
5 events/week	=	dosing regimen from the study
7 hours/day	=	dosing regimen from the study
0.26 m^3/day	=	rat inhalation rate
0.3	=	absorption efficiency
0.35 kg	=	rat body weight
168 hrs/week	=	Conversion factor

The AD_{rat} may be converted to an allowable *human* absorbed subchronic reference dose equivalent through the application of standard uncertainty factors:

UF₁ = 10 = animal -> human extrapolation

UF₂ = 10 = sensitive subpopulations

$$\text{RfD}_{\text{subchronic}} = 19 \text{ mg/kg/day} * (1/10) * (1/10)$$

$$\text{RfD}_{\text{subchronic}} = 0.2 \text{ mg/kg/day}$$

CHRONIC ORAL REFERENCE DOSE

The chronic oral Reference Dose (RfD) equivalent was derived from the combination of studies described above. The AD_{rat} calculated above may be converted to an allowable *human* absorbed chronic reference dose equivalent through the application of standard uncertainty factors:

UF₁ = 10 = animal -> human extrapolation

UF₂ = 10 = sensitive subpopulations

UF₃ = 10 = subchronic -> chronic

$$\text{RfD}_{\text{chronic}} = 19 \text{ mg/kg/day} * (1/10) * (1/10) * (1/10)$$

$$\text{RfD}_{\text{chronic}} = 0.02 \text{ mg/kg/day}$$

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ETHYLENE DIBROMIDE

SUBCHRONIC INHALATION REFERENCE CONCENTRATION

A subchronic reference concentration (RfC) equivalent value has been developed for ethylene dibromide (EDB) based on available human and animal toxicological information. Inhalation of EDB vapor may cause severe acute respiratory injury, central nervous system depression and severe vomiting (Sittig, 1981). Animal studies have indicated that EDB may produce liver and kidney injury (Sittig, 1981). EDB has been found to be a potent carcinogen in animals and has tested positively in a number of in vitro mutagenicity assays (NIOSH, 1977). In addition, EDB has produced developmental and reproductive effects in animals (NIOSH, 1977).

A thorough literature search was conducted for this compound. Most of the studies retrieved focused on carcinogenicity. The majority of studies located are summarized in the NIOSH Criteria for a Recommended Standard . . . Occupational Exposure to Ethylene Dibromide (NIOSH, 1977) and the Agency for Toxic Substances and Disease Registry Toxicological Profile for 1,2-Dibromoethane (ATSDR, 1991). Other noncarcinogenic studies identified which were not cited in the above publications include:

<u>Source</u>	<u>Species</u>	<u>Exp. Route</u>	<u>Duration</u>	<u>Effect</u>	<u>Exp. Level</u>
Williams et al., 1991	New Zeal. white rabbit	subcut.	5 days	incr. mortality; liver damage; signif. decr. sperm velocity; incr. sperm abnormalities	45 mg/kg/day (LOAEL)
NTP, 1982	mice, rats	inhal.	6 hr/d, 5 d/wk, 13 wks	decr. weight-male rats and male/female mice	3 ppm (LOAEL)

A critical subchronic inhalation study (NTP, 1982) was identified from this search. In this study, mice and rats were exposed to EDB by inhalation at concentrations of 0, 3, 15, or 75 ppm for 6 hours per day, 5 days per week for 13 weeks. The study produced a dose-related depression in weight in male rats and in male and female mice. A LOAEL of 3 ppm was identified from this study as the basis for developing a subchronic inhalation RfC using EPA RfC methodology (EPA, 1990). The following adjustments were made:

- Animal LOAEL (subchronic) = 3 ppm
- Corrected for continuous exposure over the subchronic period ($\times 6 \text{ hrs}/24 \text{ hrs} \times 5 \text{ days}/7 \text{ days}$) = 0.54 ppm
- Converted to mg/m^3 (based on $\text{mg}/\text{m}^3 = \text{ppm} \times \text{M.W.}/24.45$) = $4.1 \text{ mg}/\text{m}^3$
(Molecular Weight, M.W. = 187.88)
- Human-Equivalent Concentration (to account for absorption: (based on comparison to a rat since yields the more conservative results of the test species used: $\times 2.9^1$)) = $11.9 \text{ mg}/\text{m}^3$
- Human-Equivalent Concentration (to account for distribution, metabolism and excretion: $\div 10$) = $1.2 \text{ mg}/\text{m}^3$
- Human NOAEL ($\div 10$) = $0.12 \text{ mg}/\text{m}^3$
- Adjust for sensitive individual ($\div 10$) = $0.012 \text{ mg}/\text{m}^3$
- Low confidence in database ($\div 10$) = $0.0012 \text{ mg}/\text{m}^3$

$$\text{SUBCHRONIC RfC} = 1.2 \mu\text{g}/\text{m}^3$$

CHRONIC INHALATION REFERENCE CONCENTRATION

The Chemical Health Effects Assessment Methodology (CHEM) (MA DEP, 1990) can be used to derive a threshold effects exposure limit (TEL) which represents a concentration in air to which the general public can be exposed day after day for a lifetime and experience no adverse threshold health effects. The TEL incorporates a relative source contribution factor which, when removed, results in an Allowable Threshold Concentration (ATC) (MA DEQE, 1989). The ATC, therefore, is analogous to a chronic RfC.

Occupational limits are used as the basis for a TEL rather than primary toxicity studies. The OSHA occupational limit of 20 ppb (NIOSH 1978) was selected as the most appropriate occupational exposure limit (MAOL) for ethylene dibromide. The MAOL value was adjusted to account for continuous exposure and for protection of children and high-risk groups to derive an adjusted MAOL of $0.2 \mu\text{g}/\text{m}^3$.

- MAOL = 20 ppb
- Converted to $\mu\text{g}/\text{m}^3$ (based on $\mu\text{g}/\text{m}^3 = \text{ppb} \times \text{M.W.}/24.45$) = $153.7 \mu\text{g}/\text{m}^3$
- Adjustment for continuous exposure ($\div 4.2$) = $36.6 \mu\text{g}/\text{m}^3$
- Adjustment for childhood exposure ($\div 1.75$) = $20.9 \mu\text{g}/\text{m}^3$
- Adjustment for high-risk groups ($\div 10$) = $2.1 \mu\text{g}/\text{m}^3$

$$\text{Adjusted MAOL} = 2.1 \mu\text{g}/\text{m}^3$$

¹ According to EPA RfC methodology for gases, the air concentration should be adjusted to yield a human-equivalent concentration based on the ratio of alveolar ventilation rate divided by the body weight of the animal species to the same parameters for humans. The following formula was used:

$$(\text{Inhalation Rate}_{\text{rat}}/\text{Body Weight}_{\text{rat}})/(\text{Inhalation Rate}_{\text{human}}/\text{Body Weight}_{\text{human}})$$

The values used in the above formula include inhalation rate_{rat} = $0.29 \text{ m}^3/\text{day}$; body weight_{rat} = 0.35 kg; inhalation rate_{human} = $20 \text{ m}^3/\text{day}$; body weight_{human} = 70 kg

The adjusted MAOL was further modified to account for reproductive/developmental effects not accounted for in setting the occupational exposure limit and for relative source contribution (which is also not considered in the derivation of the occupational limit). Based on available developmental and reproductive studies, EDB was given a hazard score of "A" and assigned a threshold effects uncertainty factor (TEUF) of 10.

- TEUF adjustment (+ 10) = $0.2 \mu\text{g}/\text{m}^3$
- Relative source contribution (x 0.2) = $0.04 \mu\text{g}/\text{m}^3$

$$\text{TEL} = 0.04 \mu\text{g}/\text{m}^3$$

Removing the relative source contribution factor of 0.2 results in the Allowable Threshold Concentration:

$$\text{ATC} = 0.2 \mu\text{g}/\text{m}^3$$

or,

$$\text{CHRONIC RfC} = 0.2 \mu\text{g}/\text{m}^3$$

SUBCHRONIC ORAL REFERENCE DOSE (RfD)

A subchronic oral reference dose (RfD) equivalent value for ethylene dibromide (EDB) has been developed based on human and animal toxicological information. Acute oral exposure to EDB has produced vomiting, abdominal pain, diarrhea, nausea, anuria and death (NIOSH, 1977). Animal studies have indicated that EDB may produce liver and kidney injury (Sittig, 1981). EDB has been found to be a potent carcinogen in animals and has tested positively in a number of in vitro mutagenicity assays (NIOSH, 1977). In addition, EDB has produced developmental and reproductive effects in animals (NIOSH, 1977).

A thorough literature search was conducted for this compound. Most of the available studies for EDB are either acute exposure studies or focus on carcinogenicity as an endpoint. The majority of studies located are summarized by NIOSH (1977) and the Agency for Toxic Substances and Disease Registry (ATSDR, 1991). Other potentially pertinent studies investigating noncarcinogenic endpoints which were not cited in the above documents include:

<u>Source</u>	<u>Species</u>	<u>Exp. Route</u>	<u>Duration</u>	<u>Effect</u>	<u>Exp. Level</u>
Williams et al., 1991	New Zeal. white rabbit	subcut.	5 days	incr. mortality; liver damage; signif. decr. sperm velocity; incr. sperm abnormalities	45 mg/kg/day (LOAEL)

Several studies (NIOSH, 1977) done by the same group of investigators which are cited in the above document focus on reproductive effects produced in bulls given oral doses of EDB. A critical subchronic study (Amir et al., 1965) was selected as the basis for developing the RfD. In this study, Israeli-Friesian bulls were given oral doses of EDB from age 4 days to 24 months. From 0 to 3 months, 2 mg/kg/day was administered via ethyl alcohol in milk. From 3-12 months, 2 mg/kg/day was dissolved in soybean oil and put into the feed. After 12 months, 4 mg/kg/day was administered orally in an oil mixture by capsule every other day. The average daily dose for this period was 2 mg/kg/day. Effects noted included abnormal spermatozoa and decreased spermatozoic density and motility. Based on the results of this study, an animal LOAEL of 2 mg/kg/day has been identified. The LOAEL has been adjusted using modified EPA RfD methodology (U.S. EPA, 1987) to derive a subchronic RfC of 0.0002 mg/kg/day.

- Animal LOAEL (subchronic) = 2 mg/kg/day
- Animal NOAEL ($\div 10$) = 0.2 mg/kg/day
- Human NOAEL ($\div 10$) = 0.02 mg/kg/day
- Adjust for sensitive individual ($\div 10$) = 0.002 mg/kg/day
- Low confidence in database ($\div 10$) = 0.0002 mg/kg/day

SUBCHRONIC RfD = 0.0002 mg/kg/day

The confidence in the database is low since there are few subchronic oral studies. Of the studies located, reproductive toxicity was the only health endpoint examined. In addition, little to no information was located regarding subchronic oral exposure in humans. No adequate dose-response data were identified. Although standard EPA RfD methodology does not include an uncertainty factor for low confidence in the database, an uncertainty factor of 10 is included in the EPA methodology for developing inhalation reference concentrations (RfCs). This factor will be adopted for development of the EDB oral RfD.

CHRONIC ORAL REFERENCE DOSE (RfD)

There were no chronic oral studies identified for EDB. Based on the approach used by EPA to extrapolate a chronic NOAEL from a subchronic NOAEL, an additional uncertainty factor of 10 was applied to the NOAEL to approximate a chronic RfD for this compound. Thus:

- Subchronic RfD = 0.0002 mg/kg/day
- Chronic RfD ($\div 10$) = 0.00002 mg/kg/day

CHRONIC RfD = 0.00002 mg/kg/day

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LEAD

CHRONIC AND SUBCHRONIC ORAL REFERENCE DOSES

The Office of Research and Standards currently recommends the use of the toxicity criteria for lead back-calculated from the promulgated National Primary Drinking Water Regulation *Action Level* of 15 µg/L (U.S. EPA, 1991).

It should be explicit in all reports using these criteria that they are *not* considered risk free levels. These criteria are described as *Regulatory Daily Doses* (RDDs) to distinguish them from the U.S. EPA's Reference Doses (which are assumed to result in no adverse effects) and the subjective term "Allowable Daily Intake".

The values are:

$$\text{RDD}_{\text{oral-subchronic}} = 7.5 \times 10^{-4} \text{ mg/kg/day}$$

$$\text{RDD}_{\text{oral-chronic}} = 7.5 \times 10^{-4} \text{ mg/kg/day}$$

The RDDs given here are absorbed doses.

The aim of this section was to identify surrogate toxicity values which can effectively be used in the evaluation c.21E disposal sites. It is understood that while these interim values are not considered to be without risk of harm to health, they are within the range of "acceptable risk" for this chemical. Many of the standards and guidelines (Table 1) used to develop the values listed in Table 2 have undergone extensive *national* public review, and the risk balancing/risk management decisions made are documented (federal drinking water standards). Others have undergone *statewide* review or none at all.

Of the seven criteria considered, the two extreme toxicity values were eliminated from further consideration: the 1991 Maximum Contaminant Level Goal was considered infeasible (the derived toxicity value is 0 mg/kg/day), and the Massachusetts Department of Public Health "*Dangerous Level in Soil*" (MA DPH) is more representative of a trigger level for a Short-Term Measure than a clean-up level (the derived value is 0.005 mg/kg/day).

Among the remaining five criteria, toxicity values range from 0.00025 mg/kg/day to 0.0025 mg/kg/day, a span of a factor of ten. Three values (from the 1985 PMCLG, the 1991 Action Level, and the ORS manipulation of the lead model) are clustered in the range 0.00075 to 0.0013 mg/kg/day (less than a factor of two). The 1991 Action Level value was chosen because:

- (1) The value is consistent with results of the back-calculation from the 1985 PMCLG and ORS manipulation of the computerized lead model,
- (2) It is back-calculated from a standard (published in its final form in the June 7, 1991 *Federal Register*) and thus represents the most recent U.S. EPA statement as to what it considers an upper limit of an "allowable" exposure,
- (3) The use of the most current drinking water standard is consistent with guidance that existing standards for lead be used to evaluate noncarcinogenic risk (U.S. EPA, 1986).

This discussion is in response to a need to include quantitative evaluations of lead in the *Residential ShortForm* pursuant to the Massachusetts Contingency Plan (MCP, 310 CMR 40). These daily intakes would be used in the absence of a U.S. EPA verified Reference Dose (RfD) or Carcinogenic Potency (Slope) Value (CPV) pending a Departmental or Bureau of Waste Site Cleanup policy addressing such exposures.

DISCUSSION

Lead is a ubiquitous environmental contaminant in Massachusetts as a result of the historical use of lead paint and leaded fuels, as well as those releases of lead regulated under the MCP. The lead problem is further complicated by its toxicity: there appears to be no concentration of lead which is free from the risk of adverse non-carcinogenic health impacts if exposure were to occur. In addition, lead is considered to be a "*probable human carcinogen*" (U.S. EPA, 1989a).

The problematical regulation of lead is not limited to the the *Residential ShortForm* or the Department's Bureau of Waste Site Cleanup assessment and remediation program, and should be the subject of a Department-wide strategy to reduce *all* potential exposures to lead in the Commonwealth. As with most complex issues, such a policy cannot be completed in a matter of months. In the interim, however, it is vital that the *Residential ShortForm* have some means of quantitatively assessing lead contamination at c.21E disposal sites.

Various U.S. EPA and Massachusetts regulatory actions concerning oral exposures to lead are summarized in Table 1. Given that no exposure to lead in the environment is risk-free, virtually all of the regulatory values presented in Table 1 involve risk management decisions which balance the potential health impacts with technical feasibility and cost considerations. The use of traditional methods of developing strictly health-based criteria or assessing risk is not currently an option in the case of lead for two reasons:

- (1) there is no No Observed Adverse Effect Level (NOAEL) which is used to derive a Reference Dose or Reference Concentration, the usual bases for regulating chemicals with non-carcinogenic effects, and
- (2) there is no Carcinogenic Potency Value, the usual basis for regulating chemicals considered to be carcinogenic.

In the absence of these toxicity values, a risk assessor may search the toxicological literature for alternative values, or derive such alternative values from any existing standards or guidelines for that chemical. The latter methodology is described in the Department's *Guidance for Disposal Site Risk Characterization and Related Phase II Activities - In Support of the Massachusetts Contingency Plan* (MA DEQE, 1989) and the U.S. EPA Region I *Supplemental Risk Assessment Guidance for the Superfund Program* (U.S. EPA 1989b). This process for deriving toxicity values has been chosen for this interim approach to assessing exposure to lead at c.21E disposal sites.

It should be noted that, in certain situations, the use of these toxicity values may indicate a need for remediation at c.21E disposal sites where lead concentrations are at or below "background" levels. The *Massachusetts Contingency Plan* addresses these circumstances in 40.545 (3)(j) 2., *Requirements When a Remedial Response Action is Necessary*. This section states that if the evaluation of risk indicates a need for remediation **and** if the levels of oil or hazardous materials which would exist in the absence of the disposal site (i.e., "background") prevent achievement of guidelines, policies or total site risk limits, **then** the achievement of such "background" levels may, upon approval of the Department, be considered to meet the requirements for a permanent solution.

Table 2 summarizes these alternative toxicity values. The derivation for the chosen level follows.

N.B.: Many of the standards and guidelines which serve as the source for these "alternative toxicity values" incorporate risk management decisions which considered factors beyond solely the potential health impacts. These values should not be considered "safe", or "risk-free" levels.

TABLE 1

U.S. EPA and MASSACHUSETTS REGULATORY ACTIONS

WATER

U.S. EPA - <u>Proposed</u> (1985) Maximum Contaminant Level Goal for Drinking Water (PMCLG)	20 µg/L
U.S. EPA/Massachusetts - Maximum Contaminant Level for Drinking Water (MCL)	50 µg/L
U.S. EPA (1991) Maximum Contaminant Level Goal for Drinking Water (MCLG)	0 µg/L
U.S. EPA (1991) NPDWR Action Level (AL) (Measured at the tap)	15 µg/L
U.S. EPA - Ambient Water Quality Criteria (AWQC) (Human Health)	50 µg/L

SOIL

Massachusetts - " <i>Dangerous Level in Soil</i> " (MA DPH)	1000 mg/kg
U.S. EPA - OSWER Lead Clean-up Levels at Superfund Sites	500 - 1000 mg/kg

TABLE 2

SUMMARY OF ALTERNATIVE ABSORBED ORAL TOXICITY VALUES FOR THE EVALUATION OF LEAD IN RISK CHARACTERIZATIONS PERFORMED UNDER THE MCP

<u>SOURCE</u>	<u>VALUE</u>
ORAL	
back-calculated from PMCLG = 20 $\mu\text{g/L}$	0.001 mg/kg/day
back-calculated from MCLG = 0 $\mu\text{g/L}$	0 mg/kg/day
back-calculated from MCL = 50 $\mu\text{g/L}$	0.0025 mg/kg/day
back-calculated from Action Level = 15 $\mu\text{g/L}$	0.00075 mg/kg/day
back-calculated from UPTAKE/BIOKINETIC MODEL	0.0013 mg/kg/day
back-calculated from MA DPH "Dangerous Level in Soil"	0.005 mg/kg/day
back-calculated from EPA OSWER Directive Levels	0.0025 mg/kg/day

DOSE ESTIMATES FROM EXISTING STANDARDS AND GUIDELINES

In the absence of a U.S. EPA verified reference dose and/or reference concentration, or equivalent published toxicity values which could be used to evaluate risk of harm to human health, guidance has been provided (MA DEQE, 1989; U.S. EPA, 1989b) to assist a risk assessor in the development of acceptable alternative dose. These alternative doses are generally back-calculated from existing standards and guidelines. While this methodology is relatively straight-forward, it is important to remember that standards and guidelines may consider other factors (such as cost and feasibility) in addition to health impacts. Alternative toxicity values calculated in this manner must be accompanied by a discussion of the basis of the standard or guideline used as a starting point.

Action Level (AL)

An Interim Maximum Contaminant Level of 0.05 mg/L was promulgated for lead by the U.S. EPA in 1980. On June 7, 1991, the U.S. EPA promulgated the National Primary Drinking Water Regulation for Lead (40 CFR Part 141 and 142, Federal Register Vol. 56 No. 110)

which established an *Action Level* of 0.015 mg/liter. The *Action Level* is triggered if more than 10% of the targeted tap samples is greater than 0.015 mg/l. [An *Action Level* is defined as that concentration of lead in water that determines, in some cases, whether a water system must install corrosion control treatment, monitor source water, replace lead service lines, and undertake a public education process.] The Action Level is a standard based on health considerations, but which also considers risk management issues such as technological or economic feasibility. The following calculations detail the derivation of an Regulatory Daily Dose (RDD) the AL (the RDD_{AL}).

$$ARDD = STND * VI \div BW$$

Where:

ARDD = Applied Regulatory Daily Dose (mg/kg/day) back-calculated from the Action Level

STND = the 1991 Action Level (AL: 0.015 mg/L)

VI = Daily Intake of Water for a Child, 1 L/day

BW = A Child's Body Weight, 10 kg

$$ARDD_{AL} = 0.015 \text{ mg/L} * 1 \text{ L/day} \div 10 \text{ kg}$$

$$ARDD_{AL} = 0.0015 \text{ mg/kg/day}$$

Assuming that 50% of the lead ingested in the drinking water is absorbed in the gastrointestinal tract, the *absorbed* Regulatory Daily Doses based upon the Action Level would be:

$$RDD_{AL} = 0.0015 \text{ mg/kg/day} * 0.5$$

$$RDD_{AL} = 0.00075 \text{ mg/kg/day}$$

REFERENCES

Guidance for Disposal Site Risk Characterization and Related Phase II Activities - In Support of the Massachusetts Contingency Plan. Massachusetts Department of Environmental Quality Engineering [Policy No. WSC/ORS-141-89] (1989).

The Massachusetts Contingency Plan. Massachusetts Department of Environmental Protection, 310 CMR 40.000.

Lead Poisoning Prevention and Control. Massachusetts Department of Public Health, 105 CMR 460.

Health Effects Assessment For Lead. U.S. Environmental Protection Agency, NTIS PB # 86 134665/AS (1986).

LEAD, U.S. Environmental Protection Agency, *Integrated Risk Information System* (IRIS) file (1989a).

Supplemental Risk Assessment Guidance for the Superfund Program. U.S. Environmental Protection Agency, Region I (1989b).

National Primary Drinking Water Regulation for Lead, 40 CFR Part 141 and 142, U.S. Environmental Protection Agency, **Federal Register** 56(110).

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METHYL TERTIARY BUTYL ETHER (MTBE)

SUBCHRONIC ORAL REFERENCE DOSE

The subchronic oral Reference Dose equivalent value was derived from information presented in the U.S. EPA's Methyl-t-Butyl Ether Health Advisory (U.S. EPA, 1989). The subchronic RfD is based on a 13-week inhalation study (Greenough, 1980) in which rats were exposed for 6 hours/day, 5 days/week for 13 weeks to 0, 250, 500 or 1,000 ppm MTBE. No effects were seen on survival, body weight, hematological, clinical chemistry or urinalysis values, or gross or microscopic appearance of tissues or organs. A slight reduction in absolute and relative lung weight was observed in females exposed to 1,000 ppm MTBE. The only other effect noted by the investigators was an increasing depth of anesthesia with increasing exposure concentration. Exposure-effect relationships for anesthesia were not further delineated. Accordingly, 250 ppm is considered a LOAEL for anesthetic effects.

Based on this data, and assuming 50% absorption of inhaled methyl tert-butyl ether, a subchronic RfD equivalent may be calculated:

$$\text{LOAEL}_{13 \text{ week exposure}} = 250 \text{ ppm (901 mg/m}^3\text{)}$$

$$\text{AD}_{\text{rat}} = \frac{901 \text{ mg/m}^3 * 5 \text{ ev/wk} * 6 \text{ hr/ev} * 0.217 \text{ m}^3/\text{d} * 0.5}{0.336 \text{ kg} * 168 \text{ hr/1 wk}}$$

$$\text{AD}_{\text{rat}} = 52 \text{ mg/kg/day}$$

Where:

AD_{rat} = The calculated Absorbed Dose in the rat study. In units: mg/kg/day
 901 mg/m^3 = Lowest Observed Adverse Effects Level (LOAEL)
5 events/week = dosing regimen from the study
6 hours/day = dosing regimen from the study
 $0.217 \text{ m}^3/\text{day}$ = rat inhalation rate (based on measured body weight)
0.5 = absorption efficiency
 0.336 kg = rat body weight from study
168 hrs/week = Conversion factor

The AD_{rat} may be converted to an allowable *human* absorbed subchronic reference dose equivalent through the application of standard uncertainty factors:

$\text{UF}_1 = 10$ = animal -> human extrapolation
 $\text{UF}_2 = 10$ = sensitive subpopulations
 $\text{UF}_3 = 10$ = LOAEL -> NOAEL

$$RfD_{\text{subchronic}} = 52 \text{ mg/kg/day} * (1/10) * (1/10) * (1/10)$$

$$RfD_{\text{subchronic}} = 0.052 \text{ mg/kg/day}$$

CHRONIC ORAL REFERENCE DOSE

The chronic oral Reference Dose (RfD) equivalent was derived from the Greenough study described above. The AD_{rat} calculated above may be converted to an allowable *human* absorbed chronic reference dose equivalent through the application of standard uncertainty factors:

$UF_1 = 10 = \text{animal} \rightarrow \text{human extrapolation}$

$UF_2 = 10 = \text{sensitive subpopulations}$

$UF_3 = 10 = \text{subchronic} \rightarrow \text{chronic}$

$UF_4 = 10 = \text{LOAEL} \rightarrow \text{NOAEL}$

$$RfD_{\text{chronic}} = 52 \text{ mg/kg/day} * (1/10) * (1/10) * (1/10) * (1/10)$$

$$RfD_{\text{chronic}} = 0.0052 \text{ mg/kg/day}$$

REFERENCES

Methyl tertiary-butyl ether (Driverton) three month inhalation toxicity in rats. Greenough, R.J., P. Mc Donald, P. Robinson, J.R. Cowie, W. Maule, F. Macnaughton, and A. Rushton, Project No. 413038. Unpublished report submitted to Chemische Werke Hols, AG. Marl, West Germany. 230pp. (1980)

Methyl-t-Butyl Ether Health Advisory, U.S. Environmental Protection Agency, Office of Drinking Water (1989).

POLYCHLORINATED BIPHENYLS

CHRONIC ORAL REFERENCE DOSE

The chronic oral reference dose equivalent value for polychlorinated biphenyls (PCBs) was developed with information contained in the (DRAFT) Toxicological Profile for Selected PCBs (ATSDR, 1991). One study (Tryphonas et al., 1989) looked at several immunological parameters in monkeys fed dietary doses of Aroclor 1254 ranging from 0.005 to 0.08 mg/kg/day over a period of 133 weeks (27 months). All doses tested induced a significant and dose-related decrease in antibody levels (IgG and IgM) in response to immunization with SRBC-7, 14 and 21 days after immunization. The ATSDR calculated a "*Minimal Risk Level*" (MRL) of 0.005 µg/kg/day based upon this study in a manner similar to that described below.

$$\text{LOAEL} = 0.005 \text{ mg/kg/day}$$

$$\text{UF}_1 = 10 = \text{LOAEL to NOAEL extrapolation}$$

$$\text{UF}_2 = 10 = \text{animal} \rightarrow \text{human extrapolation}$$

$$\text{UF}_3 = 10 = \text{sensitive subpopulations}$$

$$\text{RfD}_{\text{oral-chronic}} = 0.005 \text{ mg/kg/day} * (1/10) * (1/10) * (1/10)$$

$$\text{RfD}_{\text{oral-chronic}} = 5 \times 10^{-6} \text{ mg/kg/day}$$

SUBCHRONIC ORAL REFERENCE DOSE

The chronic oral RfD equivalent derived above is based upon immunological effects which have been demonstrated following shorter exposures periods (Loose et al., 1978a, 1978b; Thomas and Hinsdill, 1978; Truelove et al., 1982) without the demonstration of a NOAEL. As a result, the chronic oral RfD equivalent has been adopted as the subchronic oral RfD equivalent.

$$\text{RfD}_{\text{oral-subchronic}} = 5 \times 10^{-6} \text{ mg/kg/day}$$

REFERENCES

DRAFT Toxicological Profile for Selected PCBs, Agency for Toxic Substances and Disease Registry, U.S. Public Health Service (1991).

Loose, L.D., Silkworth, J.B., Pittman, K.A., et al. (1978a) *Impaired host resistance to endotoxin and malaria in polychlorinated biphenyl- and hexachlorobenzene-treated mice.* **Infection and Immunity** 20:30-35.

Loose, L.D., Pittman, K.A., Benitz, K.F., et al. (1978b) *Environmental chemical-induced immune dysfunction.* **Ecotoxicol Environ Safety** 2:173-198.

Thomas, P.T. and Hinsdill, R.D. (1978) *Effect of polychlorinated biphenyls on the immune responses of rhesus monkeys and mice.* **Toxicol Appl Pharmacol** 44:41-51.

Truelove, J., Grant, D., Mes, J. et al. (1982) *Polychlorinated biphenyl toxicity in the pregnant cynomolgus monkey: A pilot study.* **Arch Environ Contam Toxicol** 11:583-588.

Tryphonas, H., Hayward, S., O'Grady, L., et al. (1989) *Immunotoxicity studies of PCB (Aroclor 1254) in the adult rhesus (Macaca mulatta) monkey -- preliminary report.* **Int J Immunopharmacol** 11:199-206.

TRICHLOROETHYLENE

SUBCHRONIC ORAL REFERENCE DOSE

The subchronic oral Reference Dose equivalent value was derived from information presented in the U.S. EPA's Trichloroethylene Health Advisory (U.S. EPA, 1987). The subchronic RfD is based on a subacute inhalation study (Kimmerle, 1973). In this study rats were exposed to 55 ppm trichloroethylene for 8 hours/day, 5 days/week for 14 weeks. Indices of toxicity include hematological investigation, liver and renal function tests, blood glucose and organ/body weight ratios. Liver weights were shown to be elevated while other test values were not different from controls. The elevated liver weights could be interpreted to be the result of hydropic changes or fatty accumulation. The no-observed-effect level was not identified since only a single concentration was administered

Based on this data, and assuming 30% absorption of inhaled trichloroethylene, a subchronic RfD equivalent may be calculated:

$$\text{LOAEL}_{14 \text{ week exposure}} = 55 \text{ ppm (300 mg/m}^3\text{)}$$

$$\text{AD}_{\text{rat}} = \frac{300 \text{ mg/m}^3 * 5 \text{ ev/wk} * 8 \text{ hr/ev} * 0.26 \text{ m}^3/\text{d} * 0.3}{0.35 \text{ kg} * 168 \text{ hr/1 wk}}$$

$$\text{AD}_{\text{rat}} = 16 \text{ mg/kg/day}$$

Where:

AD_{rat} = The calculated Absorbed Dose in the rat study. In units: mg/kg/day
 300 mg/m^3 = Lowest Observed Adverse Effects Level (LOAEL)
5 events/week = dosing regimen from the study
8 hours/day = dosing regimen from the study
 $0.26 \text{ m}^3/\text{day}$ = rat inhalation rate
0.3 = absorption efficiency
0.35 kg = rat body weight
168 hrs/week = Conversion factor

The AD_{rat} may be converted to an allowable *human* absorbed subchronic reference dose equivalent through the application of standard uncertainty factors:

$\text{UF}_1 = 10$ = animal -> human extrapolation

$\text{UF}_2 = 10$ = sensitive subpopulations

$\text{UF}_3 = 10$ = LOAEL -> NOAEL

$$\text{RfD}_{\text{subchronic}} = 16 \text{ mg/kg/day} * (1/10) * (1/10) * (1/10)$$

$$\text{RfD}_{\text{subchronic}} = 0.02 \text{ mg/kg/day}$$

CHRONIC ORAL REFERENCE DOSE

The chronic oral Reference Dose (RfD) equivalent was derived from the Kimmerle study described above. The AD_{rat} calculated above may be converted to an allowable *human* absorbed chronic reference dose equivalent through the application of standard uncertainty factors:

$\text{UF}_1 = 10 = \text{animal} \rightarrow \text{human extrapolation}$

$\text{UF}_2 = 10 = \text{sensitive subpopulations}$

$\text{UF}_3 = 10 = \text{subchronic} \rightarrow \text{chronic}$

$\text{UF}_4 = 10 = \text{LOAEL} \rightarrow \text{NOAEL}$

$$\text{RfD}_{\text{chronic}} = 16 \text{ mg/kg/day} * (1/10) * (1/10) * (1/10) * (1/10)$$

$$\text{RfD}_{\text{chronic}} = 0.002 \text{ mg/kg/day}$$

REFERENCES

Kimmerle, G. and Eben, A. (1973) *Metabolism, excretion and toxicology of trichloroethylene after inhalation. 1. Experimental exposure on rats. Arch. Toxicol.* 30:115.

Trichloroethylene Health Advisory, U.S. Environmental Protection Agency, Office of Drinking Water (1987).

VINYL CHLORIDE

CHRONIC ORAL REFERENCE DOSE

The chronic oral Reference Dose equivalent value was derived from information presented in the U.S. EPA's Vinyl Chloride Health Advisory (U.S. EPA, 1987). The chronic RfD is based on a lifetime feeding study (Til, 1981). In this study Til extended earlier work (Feron, 1981) to include lower doses with basically the same protocol used in the latter study. Carcinogenic and noncarcinogenic effects were evident with a vinyl chloride dietary level of 1.3 mg/kg/day. At dietary levels of 0.014 and 0.13 mg/kg/day, increased incidences of basophilic foci of cellular alteration in the liver of female rats were evident. However, basophilic foci by themselves are concluded not to represent an adverse effect on the liver in the absence of additional effects indicative of liver lesions such as those found in the 1.3 mg/kg/day group; and a dose-related increase in basophilic foci was not evident. Therefore, the dose of 0.13 mg/kg/day is identified as the NOAEL for noncarcinogenic effects.

Based on this data, a chronic RfD equivalent may be calculated:

$$\text{NOAEL}_{\text{rat-lifetime exposure}} = 0.13 \text{ mg/kg/day (applied dose)}$$

The $\text{NOAEL}_{\text{rat-lifetime}}$ may be converted to an allowable *human* applied chronic reference dose equivalent through the application of standard uncertainty factors:

$$\text{UF}_1 = 10 = \text{animal} \rightarrow \text{human extrapolation}$$

$$\text{UF}_2 = 10 = \text{sensitive subpopulations}$$

$$\text{RfD}_{\text{chronic}} = 0.13 \text{ mg/kg/day} * (1/10) * (1/10)$$

$$\text{RfD}_{\text{chronic}} = 0.001 \text{ mg/kg/day (applied dose)}$$

SUBCHRONIC ORAL REFERENCE DOSE

The chronic oral RfD is assumed to be protective of subchronic exposures, and the subchronic oral RfD is set equal to the chronic oral RfD.

$$\text{RfD}_{\text{subchronic}} = 0.001 \text{ mg/kg/day (applied dose)}$$

REFERENCES

Feron, V.J., Hendrikson, C.F.M., Speek, A.J., Til, H.P. and Spit, B.J. (1981) *Lifespan oral toxicity study of vinyl chloride in rats*. **Fd. Cosmet. Toxicol.** 19:317-331.

Til, H.P., Immel, H.R. and Feron, V.J. (1983) *Lifespan oral carcinogenicity study of vinyl chloride in rats*. Final Report, **Civo Institutes TNO**. Report No. V 83.285/291099.

Vinyl Chloride Health Advisory, U.S. Environmental Protection Agency, Office of Drinking Water (1987).

APPENDIX E

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